I CLAIM:

1. A method of patterned data analysis for monitoring individual metabolic response and for generating predictive clinical metrics on HATR-FTIR spectroscopy by determining spectral characteristics of glucemic variability (GV) for healthy, prediabetic and diabetic subjects, except for human beings, consisting of:

(i) assigning glucose-specific peaks with characteristic absorption wave numbers at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the 700-4000 cm^{-1} region in gathered HATR-FTIR spectra from the forearm of a tested subject, except for human being, under post-prandial glucose test or OGTT (oral glucose tolerance test) with different doses at 5 g, 20 g and 75 g, wherein spectrally assigned glucose-specific peaks at 1030 cm^{-1} and 1041 cm^{-1} are always bounded bands together;

(ii) determining spectral characteristics of glucemic variability (GV) for each assigned glucose-specific peak in correlation with the peak position and its shift to the left or to the right in HATR-FTIR spectra, wherein shifts of the peak position at 1030 - 1041 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are characteristic for healthy, prediabetic and diabetic subjects, except for human beings, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g;

(iii) determining spectral characteristics of GV for each assigned glucose-specific peak in correlation with the peak level in HATR-FTIR spectra, wherein determination of the highest peak level at 1030 - 1041 cm^{-1} and determination of the highest peak level among all assigned glucose-specific peaks is characteristic for healthy, prediabetic and diabetic subjects, except for human beings, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g;

(iv) determining spectral characteristics of GV for each assigned glucose-specific peak in correlation with dose-dependent dynamic changes of the peak level under a continuous 120-minute test monitoring at pre-determined time-intervals from the starting till the ending time-points under comparative OGTT test with 5 g, 20 g and 75 g glucose, wherein the levels of the peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are independent to intaken dose of glucose under OGTT at 5 g (low), 20 g (medium) and 75 g (high) in healthy subjects, the levels of the peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are dependent to intaken dose of glucose under OGTT at 5 g (low), 20 g (medium) and 75 g (high) in prediabetic and diabetic subjects, except for human beings;

(v) recognizing the spectral pattern of individual metabolic response by a continuous monitoring of GV, to be specific for healthy, prediabetic and diabetic subjects, except for human beings, wherein

the spectral pattern with predominant left-shifted mean peak position towards 1030 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 8 c-e and Figure 11 a, predominant left-shifted mean peak position towards 1116-1118 cm^{-1} at 1118 cm^{-1} according to Figure 5 c and Figure 7 a, predominant left-shifted mean peak position towards 1149-1153 cm^{-1} at 1153 cm^{-1} according to Figure 8 e and Figure 11 d, highest glucose peak levels at 1030-1041 cm^{-1} over for peaks levels at 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} according to Figure 8 c-e, lowest glucose peak levels at 1153 cm^{-1} below peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 e, independent to intaken glucose dose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 5 g (low), 20 g (medium) and 75 g (high) according to Figure 5 a-c, to be specific for a healthy subject, except for human being, or

the spectral pattern with predominant right-shifted mean peak position towards 1037-1041 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 8 f and Figure 11 a, predominant right-shifted mean peak position towards 1120-1122 cm^{-1} at 1118 cm^{-1} according to Figure 11 c, similarly high peak levels at 1030-1041 cm^{-1} and at 1118 cm^{-1} over for peak levels at 1080 cm^{-1} and 1153 cm^{-1} according to Figure 8 f, lowest glucose peak levels at 1153 cm^{-1} below peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 11 d, dependent to intaken glucose dose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} under OGTT at 5 g (low), 20 g (medium) and 75 g (high) according to Figure 11 a-c, to be specific for a prediabetic subject, except for human being, or

the spectral pattern with dominant right-shifted mean peak position towards 1041 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 6 a, 8 a-b and 11 a, dominant right-shifted mean peak position towards 1120-1122 cm^{-1} at 1118 cm^{-1} according to Figure 6 c, dominant right-shifted mean peak position towards 1153-1157 cm^{-1} at 1153 cm^{-1} according to Figure 8 b, highest glucose peak levels at 1118 cm^{-1} over for peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1153 cm^{-1} according to Figure 8 b, lowest glucose peak levels at 1153 cm^{-1} below peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 b, dependent to intaken glucose dose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} under OGTT at 5 g (low), 20 g (medium) and 75 g (high) according to Figure 6 a-c, to be specific for a diabetic subject with type 2, except for human being.

2. A method of patterned data analysis for monitoring individual metabolic response and for generating predictive clinical metrics on HATR-FTIR spectroscopy by determining spectral characteristics of the latency time for healthy, prediabetic and diabetic subjects, except for human beings, consisting of:

(i) assigning glucose-specific peaks with characteristic absorption wave numbers at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the 700-4000 cm^{-1} region in gathered HATR-FTIR spectra from the forearm of a tested subject, except for human being, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g, wherein spectrally assigned glucose-specific peaks at 1030 cm^{-1} and 1041 cm^{-1} are always bounded bands together;

(ii) calculating the latency time (LT) duration for each assigned glucose-specific peak at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, wherein said LT is the time interval from the time-point of induction of glucose excursions till the time-point of maximum detected levels of said glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on HATR-FTIR spectrometer in the interstitial fluid of skin tissue;

(iii) comparing calculated LT duration for each assigned glucose-specific peak at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the interstitial fluid of skin tissue with the LT duration in capillary blood glucose (CBG) gathered in the same subject, except for human being, by calculating the LT differences, wherein said LT is the time interval from the time-point of induction of glucose excursions till the time-point of maximum detected levels of said CBG measurements in said subject in capillary blood glucose;

(iv) determining spectral characteristics for calculated LT and LT's difference intervals for each assigned glucose-specific peak in correlation with their durations, wherein the shortest and the longest intervals in minutes to be specific for healthy, prediabetic and diabetic subjects, except for human beings;

(v) determining spectral characteristics for calculated LT and LT's difference intervals for each assigned glucose-specific peak in correlation with their phasic appearances, wherein single, bi-phasic and cascading multi-phase appearance to be specific for healthy, prediabetic and diabetic subjects, except for human beings;

(vi) determining spectral characteristics for calculated LT and LT's difference intervals for each assigned glucose-specific peak in correlation with dose-dependency, to be specific for healthy, prediabetic and diabetic subjects, except for human beings;

(vii) determining the spectral pattern of individual metabolic response by calculating LT and LT's difference intervals for each assigned glucose-specific peak under post-prandial glucose test and OGTT with different doses at 5 g, 20 g and 75 g, to be specific for healthy, prediabetic and diabetic subjects, except for human beings, wherein

the spectral pattern characterized by

bi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 15` and 30` under OGTT at 5 g according to Table 2 (column 3, row 2),

single-phase LTs and LT's differences at 1030-1041 cm^{-1} of 10` under OGTT at 20 g according to Table 2 (column 4, row 2),

bi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 5`and 30`under OGTT at 75 g according to Table 2 (column 5, row 2),

bi-phase LTs and LT's differences at 1080 cm^{-1} of 15` and 30` under OGTT at 5 g according to Table 2 (column 3, row 3),

cascading multi-phase LTs and LT's differences at 1080 cm^{-1} of 0`, 10`and 20` under OGTT at 20 g according to Table 2 (column 4, row 3),

single-phase LTs and LT's differences at 1080 cm^{-1} of 5` under OGTT at 75 g according to Table 2 (column 5, row 3),

bi-phase LTs and LT's differences at 1118 cm^{-1} of 10` and 25` under OGTT at 5 g according to Table 2 (column 3, row 4),

single-phase LT and LT's difference at 1118 cm^{-1} of 10` under OGTT at 20 g according to Table 2 (column 4, row 4),

bi-phase LTs and LT's differences at 1118 cm^{-1} of 5` and 25` under OGTT at 75 g according to Table 2 (column 5, row 4),

bi-phase LTs and LT's differences at 1153 cm^{-1} of 35` and 50` under OGTT at 5 g according to Table 2 (column 3, row 5),

single-phase LT and LT's difference at 1153 cm^{-1} of 10`and 15` under OGTT at 20 g according to Table 2 (column 4, row 5),

single-phase LT and LT's difference at 1153 cm^{-1} of 30` under OGTT at 75 g according to Table 3 (column 5, row 5),

the longest durations of LT's differences of

5`& 30` (75 g), 10` (20 g) and 15`& 30` (5 g) at 1030-1041 cm^{-1},

5` (75 g), 0`& 10`& 20` (20 g) and 15`& 30` (5 g) at 1080 cm^{-1},

5`& 25` (75 g), 10` (20 g) and 10`& 25` (5 g) at 1118 cm^{-1},

10` (75 g), 10` & 15` (20 g) and 35`and 50` at 1153 cm^{-1}

under OGTT with different doses according to Table 2,

dose-independent LTs and LT's differences for each assigned glucose-specific peak under any OGTT with different doses of 5 g, 20 g or 75 g,

bi-phase LTs with LT's differences of 15` & 30` at 1030-1041 cm^{-1}, 15` & 30` at 1080 cm^{-1}, 10` & 25` at 1118 cm^{-1}, 35` & 50` at 1153 cm^{-1} under OGTT at 5 g according to Table 2 (column 3),

single-, bi-phase and cascading multi-phase LTs with LT's differences of 10` at 1030-1041 cm$^{-1}$, 0` & 10` and 20` at 1080 cm^{-1}, 10`at 1118 cm$^{-1}$, 10` & 15`at 1153 cm^{-1} under OGTT at 20 g according to Table 2 (column 4),

single- and bi-phase LTs with LT's differences of 5`& 30`at 1030-1041 cm^{-1}, 5` at 1080 cm$^{-1}$, 5`& 25`at 1118 cm$^{-1}$, 10` at 1153 cm^{-1} under OGTT at 75 g according to Table 2 (column 5),

the longest durations of LT's differences starting from 5`with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a healthy subject, except for human being, according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2),

as compared with the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a diabetic subject, except for human being, according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4), and

as compared with the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a prediabetic subject, except for human being, according to Table 7 (column 3),

to be specific for a healthy subject, except for human being, or

the spectral pattern characterized by

cascading multi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 5`, 20`, 30` & 45` under OGTT at 75 g according to Table 7 (column 3, row 2),

cascading multi-phase LTs and LT's differences at 1080 cm^{-1} of 5`, 20` & 45` under OGTT at 75 g according to Table 7 (column 3, row 3),

cascading multi-phase LTs and LT's differences at 1118 cm^{-1} of 5`, 20`, 30` & 40` under OGTT at 75 g according to Table 7 (column 3, row 4),

cascading multi-phase LTs and LT's differences at 1153 cm^{-1} of 0`, 15`, 25` & 55` under OGTT at 75 g according to Table 7 (column 3, row 5),

cascading multi-phase LTs and LT's differences of 5`- 45` at 1030-1041 cm^{-1}, 5`- 45` at 1080 cm^{-1}, 5`- 40` at 1118 cm^{-1}, 0`- 55` at 1153 cm^{-1} under OGTT at 75 g,

dose-independent LTs and LT's differences with cascading multi-phase appearances at

5`, 20`, 30` & 45` at 1030-1041 cm^{-1},

5`, 20` & 45` at 1080 cm^{-1},

5`, 20`, 30` & 40` at 1118 cm^{-1},

0`, 15`, 25` & 55` at 1153 cm^{-1}

under OGTT at 75 g according to Table 7 (column 3, rows 2-5),

the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g according to Table 7 (column 3),

as compared with the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75

g in a diabetic subject, except for human being, according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4), and

as compared with the longest durations of LT's differences starting from 5` with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a healthy subject according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2), to be specific for a prediabetic subject, except for human being, or

the spectral pattern characterized by

bi-phase LTs and LT's differences of 0` & 10` at 1030-1041 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 2),

single-phase LT and LT's difference of 0` at 1030-1041 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 2),

single-phase LT and LT's difference of 0` at 1030-1041 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 2),

single-phase LT and LT's difference of 10` at 1080 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 3),

single-phase LT and LT's difference of 15` at 1080 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 3),

single-phase LT and LT's difference of 0` at 1080 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 3) and to Table 7 (column 4, row 3),

cascading multi-phase LTs and LT's differences of 0`, 10` & 25` at 1118 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 4),

single-phase LT and LT's difference of 5` at 1118 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 4),

single-phase LT and LT's difference of 0` at 1118 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 4),

bi-phase LTs and LT's differences of 15` & 25` under OGTT at 5 g according to Table 3 (column 3, row 5),

bi-phase LTs and LT's differences of 25` & 40` under OGTT at 20 g according to Table 3 (column 4, row 5),

single-phase LT and LT's differences of 30` under OGTT at 75 g according to Table 3 (column 5, row 5),

the shortest durations of LT's differences of

0` (75 g), 0` (20 g), 0` & 10` (5 g) at 1030-1041 cm⁻¹,

0` (75 g), 15` (20 g), 10` (5 g) at 1080 cm⁻¹,

0` (75 g), 5` (20 g), 0`& 10`& 25` (5 g) at 1118 cm⁻¹,

30` (75 g), 25` & 40` (20 g), 15`& 25` at 1153 cm⁻¹

under OGTT with different doses according to Table 3,

the shortest durations of LTs and LT's differences of

0` at 1030-1041 cm⁻¹,

0`, 0`& 60` or 60` at 1080 cm⁻¹,

0`or 0`& 60` at 1118 cm⁻¹,

30`& 60` at 1153 cm⁻¹

under post-prandial glucose test according to Table 1,

dose-dependent LTs and LT's differences at 1030-1041 cm⁻¹, 1080 cm⁻¹ and 1118 cm⁻¹ under any OGTT with different doses at 5 g, 20 g and 75 g glucose,

single-, bi-phase and cascading multi-phase LTs and LT's differences of 0` & 10` at 1030-1041 cm⁻¹, 10` at 1080 cm⁻¹, 0`, 10` & 25` at 1118 cm⁻¹, 15` & 25` at 1153 cm⁻¹ under OGTT at 5 g according to Table 3 (column 3),

single- and bi-phase LTs and LT's differences of 0` at 1030-1041 cm⁻¹, 15' at 1080 cm⁻¹, 5' at 1118 cm⁻¹, 15'& 40' at 1153 cm⁻¹ under OGTT at 20 g according to Table 3 (column 4),

single-phase LT and and LT's differences of 0' at 1030-1041 cm⁻¹, 0' at 1080 cm⁻¹, 0' at 1118 cm⁻¹, 30' at 1153 cm⁻¹ under OGTT at 75 g according to Table 3 (column 5),

the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm⁻¹, 1080 cm⁻¹, 1118 cm⁻¹ and 1153 cm⁻¹ under OGTT at 75 g according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4),

as compared with the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm⁻¹, 1080 cm⁻¹, 1118 cm⁻¹ and 1153 cm⁻¹ under OGTT at 75 g in a prediabetic subject, except for human being, according to Table 7 (column 3), and

as compared with the longest durations of LT's differences starting from 5` with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a healthy subject, except for human being, according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2),

to be specific for a diabetic subject with type 2, except for human being.

3. A method for monitoring the spectral pattern and the change of the spectral pattern of individual metabolic response on HATR-FTIR spectroscopy by determining spectral characteristics of glucemic variability (GV) for healthy, prediabetic and diabetic subjects, except for human beings, consisting of:

(i) assigning glucose-specific peaks with characteristic absorption wave numbers at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the 700-4000 cm^{-1} region in gathered HATR-FTIR spectra from the forearm of a tested subject, except for human beings, under post-prandial glucose test or OGTT (oral glucose tolerance test) with different doses at 5 g, 20 g and 75 g, wherein spectrally assigned glucose-specific peaks at 1030 cm^{-1} and 1041 cm^{-1} are always bounded bands together;

(ii) determining spectral characteristics of glucemic variability (GV) for each assigned glucose-specific peak in correlation with the peak position and its shift to the left or to the right in HATR-FTIR spectra, wherein shifts of the peak position at 1030 - 1041 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are characteristic for healthy, prediabetic and diabetic subjects, except for human beings, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g;

(iii) determining spectral characteristics of GV for each assigned glucose-specific peak in correlation with the peak level in HATR-FTIR spectra, wherein determination of the highest peak level at 1030 - 1041 cm^{-1} and determination of the highest peak level among all assigned glucose-specific peaks is characteristic for healthy, prediabetic and diabetic subjects, except for human beings, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g;

(iv) determining spectral characteristics of GV for each assigned glucose-specific peak in correlation with dose-dependent dynamic changes of the peak level under a continuous 120-minute test monitoring at pre-determined time-intervals from the starting till the ending time-points under comparative OGTT test with 5 g, 20 g and 75 g glucose, wherein the levels of the peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are independent to intaken dose

of glucose under OGTT at 5 g (low), 20 g (medium) and 75 g (high) in healthy subjects, the levels of the peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are dependent to intaken dose of glucose under OGTT at 5 g (low), 20 g (medium) and 75 g (high) in prediabetic and diabetic subjects, except for human beings;

(v) recognizing the spectral pattern of individual metabolic response by a continuous monitoring of GV, to be specific for healthy, prediabetic and diabetic subjects, except for human beings, wherein

the spectral pattern with predominant left-shifted mean peak position towards 1030 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 8 c-e and Figure 11 a, predominant left-shifted mean peak position towards 1116-1118 cm^{-1} at 1118 cm^{-1} according to Figure 5 c and Figure 7 a, predominant left-shifted mean peak position towards 1149-1153 cm^{-1} at 1153 cm^{-1} according to Figure 8 e and Figure 11 d, highest glucose peak levels at 1030-1041 cm^{-1} over for peaks levels at 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} according to Figure 8 c-e, lowest glucose peak levels at 1153 cm^{-1} below peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 e, independent to intaken glucose dose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 5 g (low), 20 g (medium) and 75 g (high) according to Figure 5 a-c, to be specific for a healthy subject, except for human being, or

the spectral pattern with predominant right-shifted mean peak position towards 1037-1041 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 8 f and Figure 11 a, predominant right-shifted mean peak position towards 1120-1122 cm^{-1} at 1118 cm^{-1} according to Figure 11 c, similarly high peak levels at 1030-1041 cm^{-1} and at 1118 cm^{-1} over for peak levels at 1080 cm^{-1} and 1153 cm^{-1} according to Figure 8 f, lowest glucose peak levels at 1153 cm^{-1} below peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 11 d, dependent to intaken glucose dose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} under OGTT at 5 g (low), 20 g (medium) and 75 g (high) according to Figure 11 a-c, to be specific for a prediabetic subject, except for human being, or

the spectral pattern with dominant right-shifted mean peak position towards 1041 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 6 a, 8 a-b and 11 a, dominant right-shifted mean peak position towards 1120-1122 cm^{-1} at 1118 cm^{-1} according to Figure 6 c, dominant right-shifted mean peak position towards 1153-1157 cm^{-1} at 1153 cm^{-1} according to Figure 8 b, highest glucose peak levels at 1118 cm^{-1} over for peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1153 cm^{-1} according to Figure 8 b, lowest glucose peak levels at 1153 cm^{-1} below peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 b, dependent to intaken glucose

dose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} under OGTT at 5 g (low), 20 g (medium) and 75 g (high) according to Figure 6 a-c, to be specific for a diabetic subject with type 2, except for human being.

4. A method for monitoring the spectral pattern and the change of the spectral pattern of individual metabolic response on HATR-FTIR spectroscopy by determining spectral characteristics of the latency time (LT) for healthy, prediabetic and diabetic subjects, except for human beings, consisting of:

(i) assigning glucose-specific peaks with characteristic absorption wave numbers at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the 700-4000 cm^{-1} region in gathered HATR-FTIR spectra from the forearm of a tested subject, except for human being, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g, wherein spectrally assigned glucose-specific peaks at 1030 cm^{-1} and 1041 cm^{-1} are always bounded bands together;

(ii) calculating the latency time (LT) duration for each assigned glucose-specific peak at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, wherein said LT is the time interval from the time-point of induction of glucose excursions till the time-point of maximum detected levels of said glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on HATR-FTIR spectrometer in the interstitial fluid of skin tissue;

(iii) comparing calculated LT duration for each assigned glucose-specific peak at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the interstitial fluid of skin tissue with the LT duration in capillary blood glucose (CBG) gathered in the same subject, except for human being, by calculating the LT differences, wherein said LT is the time interval from the time-point of induction of glucose excursions till the time-point of maximum detected levels of said CBG measurements in said subject in capillary blood glucose;

(iv) determining spectral characteristics for calculated LT and LT's difference intervals for each assigned glucose-specific peak in correlation with their durations, wherein the shortest and the longest intervals in minutes to be specific for healthy, prediabetic and diabetic subjects, except for human beings;

(v) determining spectral characteristics for calculated LT and LT's difference intervals for each assigned glucose-specific peak in correlation with their phasic appearances, wherein

single, bi-phasic and cascading multi-phase appearance to be specific for healthy, prediabetic and diabetic subjects, except for human beings;

(vi) determining spectral characteristics for calculated LT and LT's difference intervals for each assigned glucose-specific peak in correlation with dose-dependency, to be specific for healthy, prediabetic and diabetic subjects, except for human beings;

(vii) determining the spectral pattern of individual metabolic response by calculating LT and LT's difference intervals for each assigned glucose-specific peak under post-prandial glucose test and OGTT with different doses at 5 g, 20 g and 75 g, to be specific for healthy, prediabetic and diabetic subjects, except for human beings, wherein

the spectral pattern characterized by

bi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 15` and 30` under OGTT at 5 g according to Table 2 (column 3, row 2),

single-phase LTs and LT's differences at 1030-1041 cm^{-1} of 10` under OGTT at 20 g according to Table 2 (column 4, row 2),

bi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 5`and 30`under OGTT at 75 g according to Table 2 (column 5, row 2),

bi-phase LTs and LT's differences at 1080 cm^{-1} of 15` and 30` under OGTT at 5 g according to Table 2 (column 3, row 3),

cascading multi-phase LTs and LT's differences at 1080 cm^{-1} of 0`, 10`and 20` under OGTT at 20 g according to Table 2 (column 4, row 3),

single-phase LTs and LT's differences at 1080 cm^{-1} of 5` under OGTT at 75 g according to Table 2 (column 5, row 3),

bi-phase LTs and LT's differences at 1118 cm^{-1} of 10` and 25` under OGTT at 5 g according to Table 2 (column 3, row 4),

single-phase LT and LT's difference at 1118 cm^{-1} of 10` under OGTT at 20 g according to Table 2 (column 4, row 4),

bi-phase LTs and LT's differences at 1118 cm^{-1} of 5` and 25` under OGTT at 75 g according to Table 2 (column 5, row 4),

bi-phase LTs and LT's differences at 1153 cm^{-1} of 35` and 50` under OGTT at 5 g according to Table 2 (column 3, row 5),

single-phase LT and LT's difference at 1153 cm^{-1} of 10`and 15` under OGTT at 20 g according to Table 2 (column 4, row 5),

single-phase LT and LT's difference at 1153 cm^{-1} of 30` under OGTT at 75 g according to Table 3 (column 5, row 5),

the longest durations of LT's differences of

5`& 30` (75 g), 10` (20 g) and 15`& 30` (5 g) at 1030-1041 cm^{-1},

5` (75 g), 0`& 10`& 20` (20 g) and 15`& 30` (5 g) at 1080 cm^{-1},

5`& 25` (75 g), 10` (20 g) and 10`& 25` (5 g) at 1118 cm^{-1},

10` (75 g), 10` & 15` (20 g) and 35`and 50` at 1153 cm^{-1}

under OGTT with different doses according to Table 2,

dose-independent LTs and LT's differences for each assigned glucose-specific peak under any OGTT with different doses of 5 g, 20 g or 75 g,

bi-phase LTs with LT's differences of 15` & 30` at 1030-1041 cm^{-1}, 15` & 30` at 1080 cm^{-1}, 10` & 25` at 1118 cm^{-1}, 35` & 50` at 1153 cm^{-1} under OGTT at 5 g according to Table 2 (column 3),

single-, bi-phase and cascading multi-phase LTs with LT's differences of 10` at 1030-1041 cm$^{-1}$, 0` & 10` and 20` at 1080 cm^{-1}, 10`at 1118 cm$^{-1}$, 10` & 15`at 1153 cm^{-1} under OGTT at 20 g according to Table 2 (column 4),

single- and bi-phase LTs with LT's differences of 5`& 30`at 1030-1041 cm^{-1}, 5` at 1080 cm$^{-1}$, 5`& 25`at 1118 cm$^{-1}$, 10` at 1153 cm^{-1} under OGTT at 75 g according to Table 2 (column 5),

the longest durations of LT's differences starting from 5`with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a healthy subject, except for human being, according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2),

as compared with the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75

g in a diabetic subject, except for human being, according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4), and

as compared with the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a prediabetic subject, except for human being, according to Table 7 (column 3),

to be specific for a healthy subject, except for human being, or

the spectral pattern characterized by

cascading multi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 5`, 20`, 30`& 45` under OGTT at 75 g according to Table 7 (column 3, row 2),

cascading multi-phase LTs and LT's differences at 1080 cm^{-1} of 5`, 20`& 45`under OGTT at 75 g according to Table 7 (column 3, row 3),

cascading multi-phase LTs and LT's differences at 1118 cm^{-1} of 5`, 20`, 30`& 40` under OGTT at 75 g according to Table 7 (column 3, row 4),

cascading multi-phase LTs and LT's differences at 1153 cm^{-1} of 0`, 15`, 25`& 55` under OGTT at 75 g according to Table 7 (column 3, row 5),

cascading multi-phase LTs and LT's differences of 5`- 45` at 1030-1041 cm^{-1}, 5`- 45` at 1080 cm^{-1}, 5`- 40` at 1118 cm^{-1}, 0`- 55` at 1153 cm^{-1} under OGTT at 75 g,

dose-independent LTs and LT's differences with cascading multi-phase appearances at

5`, 20`, 30` & 45` at 1030-1041 cm^{-1},

5`, 20` & 45` at 1080 cm^{-1},

5`, 20`, 30` & 40` at 1118 cm^{-1},

0`, 15`, 25` & 55` at 1153 cm^{-1}

under OGTT at 75 g according to Table 7 (column 3, rows 2-5),

the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g according to Table 7 (column 3),

as compared with the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a diabetic subject, except for human being, according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4), and

as compared with the longest durations of LT's differences starting from 5` with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a healthy subject according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2), to be specific for a prediabetic subject, except for human being, or

the spectral pattern characterized by

bi-phase LTs and LT's differences of 0` & 10` at 1030-1041 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 2),

single-phase LT and LT's difference of 0` at 1030-1041 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 2),

single-phase LT and LT's difference of 0` at 1030-1041 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 2),

single-phase LT and LT's difference of 10` at 1080 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 3),

single-phase LT and LT's difference of 15`at 1080 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 3),

single-phase LT and LT's difference of 0`at 1080 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 3) and to Table 7 (column 4, row 3),

cascading multi-phase LTs and LT's differences of 0`, 10` & 25` at 1118 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 4),

single-phase LT and LT's difference of 5` at 1118 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 4),

single-phase LT and LT's difference of 0` at 1118 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 4),

bi-phase LTs and LT's differences of 15`& 25` under OGTT at 5 g according to Table 3 (column 3, row 5),

bi-phase LTs and LT's differences of 25`& 40` under OGTT at 20 g according to Table 3 (column 4, row 5),

single-phase LT and LT's differences of 30` under OGTT at 75 g according to Table 3 (column 5, row 5),

the shortest durations of LT's differences of

0` (75 g), 0` (20 g), 0` & 10` (5 g) at 1030-1041 cm^{-1},

0` (75 g), 15` (20 g), 10` (5 g) at 1080 cm^{-1},

0` (75 g), 5` (20 g), 0`& 10`& 25` (5 g) at 1118 cm^{-1},

30` (75 g), 25` & 40` (20 g), 15`& 25` at 1153 cm^{-1}

under OGTT with different doses according to Table 3,

the shortest durations of LTs and LT's differences of

0` at 1030-1041 cm^{-1},

0`, 0`& 60` or 60` at 1080 cm^{-1},

0`or 0`& 60` at 1118 cm^{-1},

30`& 60` at 1153 cm^{-1}

under post-prandial glucose test according to Table 1,

dose-dependent LTs and LT's differences at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} under any OGTT with different doses at 5 g, 20 g and 75 g glucose,

single-, bi-phase and cascading multi-phase LTs and LT's differences of 0` & 10` at 1030-1041 cm^{-1}, 10` at 1080 cm$^{-1}$, 0`, 10` & 25` at 1118 cm^{-1}, 15` & 25` at 1153 cm^{-1} under OGTT at 5 g according to Table 3 (column 3),

single- and bi-phase LTs and LT's differences of 0` at 1030-1041 cm^{-1}, 15' at 1080 cm^{-1}, 5' at 1118 cm^{-1}, 15'& 40' at 1153 cm^{-1} under OGTT at 20 g according to Table 3 (column 4),

single-phase LT and and LT's differences of 0' at 1030-1041 cm^{-1}, 0' at 1080 cm^{-1}, 0' at 1118 cm^{-1}, 30' at 1153 cm^{-1} under OGTT at 75 g according to Table 3 (column 5),

the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4),

as compared with the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}

under OGTT at 75 g in a prediabetic subject, except for human being, according to Table 7 (column 3), and

as compared with the longest durations of LT's differences starting from 5` with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a healthy subject, except for human being, according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2),

to be specific for a diabetic subject with type 2, except for human being.

5. The method as claimed in any of claims 1 to 4 for diagnosing disorders of glucose metabolism including prediabetes and diabetes in a subject except for human being, or for screening and following up development of diabetes in a healthy subject except for human being, or for screening and following up development of diabetes in a subject with prediabetes except for human being, or for predicting the risk of hyperglycemia in a subject except for human being, or for staging type 2 diabetes in a subject except for human being, or for managing a subject with or without hyperglycemia except for human being, or for assessing the quality of metabolic control in a subject except for human being, or for determining an effective therapy in a subject with type 2 diabetes except for human being, or for determining effective dosage of drug in a subject with type 2 diabetes except for human being, or for stratifying a subject to therapeutic regimen for treating or preventing diabetes by determining prognosis of treatment in prediabetic and diabetic subjects except for human beings, by obtaining spectral data information comprising spectral patterns specific to healthy, prediabetes and diabetic subjects.

6. A spectral method for in vivo glucose molecule characterization at 1030 cm^{-1} or 1041 cm^{-1}, characterized in HATR-FTIR spectra by bounded bands together within 1030-1041 cm^{-1} corresponding to identity and structures to glucose molecules in correlation with characteristic measurements of the peak position and its shift, the peak levels measured in the interstitial fluid of the epidermal skin tissue of a healthy, prediabetic or diabetic subject, except for human being, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g by HATR-FTIR spectroscopy, comprising one of the following:

(i) characterizing a glucose molecule in HATR-FTIR spectra by

predominant mean peak position at 1030 cm^{-1} within 1030-1041 cm^{-1},

the highest glucose peak levels within 1030-1041 cm^{-1} over the other glucose peaks levels at 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1},

independent to low, medium and high glucose doses peak levels under OGTT with 5 g, 20 g and 75 g,

bi-phase LTs and LT's differences of 15` and 30` under OGTT at 5 g,

single-phase LTs and LT's differences of 10` under OGTT at 20 g,

bi-phase LTs and LT's differences of 5`and 30`under OGTT at 75 g,

to be specific for a healthy subject, except for human being; or

(ii) characterizing a glucose molecule in HATR-FTIR spectra by

predominant mean peak position at 1037-1041 cm^{-1} within 1030-1041 cm^{-1},

the highest glucose peak levels within 1030-1041 cm^{-1} similar to the peak levels at 1118 cm^{-1} in HATR-FTIR spectra,

dose-dependent peak levels to high doses of glucose under OGTT at 75 g,

cascading multi-phase LTs and LT's differences of 5`, 20`, 30`& 45` under OGTT at 75 g, to be specific for a prediabetic subject, except for human being; or

(iii) characterizing a glucose molecule in HATR-FTIR spectra by

predominant mean peak position at 1039-1041 cm^{-1} within 1030 - 1041 cm^{-1} in HATR-FTIR spectra,

dose-dependent to low, medium and high glucose doses peak levels under OGTT with 5 g, 20 g and 75 g,

single-phase LT and LT's difference of 0` under post-prandial glucose test,

bi-phase LTs and LT's differences of 0` & 10` under OGTT at 5 g,

single-phase LT and LT's difference of 0` under OGTT at 20 g,

single-phase LT and LT's difference of 0` under OGTT at 75 g,

to be specific for a diabetic subject, except for human being.

7. A spectral method for in vivo glucose molecule characterization at 1080 cm^{-1}, characterized by spectral bounded bands at 1080 cm^{-1} in HATR-FTIR spectra corresponding to identity and structures to glucose molecules in correlation with characteristic measurements of the peak position and its shift, the peak levels measured in the interstitial fluid of the epidermal skin tissue of a healthy, prediabetic or diabetic subject, except for human being, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g by HATR-FTIR spectroscopy, comprising one of the following:

(i) characterizing a glucose molecule in HATR-FTIR spectra by

dose-independent peak levels to low, medium and high glucose doses under OGTT with 5 g, 20 g and 75 g,

bi-phase LTs and LT's differences of 15`& 30` under OGTT at 5 g,

cascading multi-phase LTs and LTs differences of 0`, 10`& 20` under OGTT at 20 g,

single-phase LT and LT's difference of 5`under OGTT at 75 g,

to be specific for a healthy subject, except for human being; or

(ii) characterizing a glucose molecule in HATR-FTIR spectra by

dose-dependent peak levels to high glucose dose under OGTT with 75 g,

cascading multi-phase LTs and LT's differences of 5`, 20`& 45` under OGTT at 75 g,

to be specific for a prediabetic subject, except for human being; or

(iii) characterizing a glucose molecule in HATR-FTIR spectra by

dose-dependent peak levels to low, medium and high glucose doses under OGTT with 5 g, 20 g and 75 g,

single-phase LT and LT's difference of 10`under OGTT at 5 g,

single-phase LT and LT's difference of 15`under OGTT at 20 g,

single-phase LT and LT's difference of 0`under OGTT at 75 g,

to be specific for a diabetic subject, except for human being.

8. A spectral method for in vivo glucose molecule characterization at 1118 cm^{-1}, characterized by spectral bounded bands at 1118 cm^{-1} in HATR-FTIR spectra corresponding to identity and structures to glucose molecules in correlation with characteristic measurements of the peak position and its shift, the peak levels measured in the interstitial fluid of the epidermal skin tissue of a healthy, prediabetic or diabetic subject, except for human being, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g by HATR-FTIR spectroscopy, comprising one of the following:

(i) characterizing a glucose molecule in HATR-FTIR spectra by

predominant left-shifted mean peak position within 1114-1118 cm^{-1}, wherein mean peak position at 1118 cm^{-1} is characteristic under OGTT at 5 g, mean peak position at 1114-1118 cm^{-1} is characteristic under OGTT at 20 g, mean peak position at 1116-1118 cm^{-1} is characteristic under OGTT at 75 g,

dose-independent peak levels to low, medium and high glucose doses under OGTT with 5 g, 20 g and 75 g,

bi-phase LTs and LT's differences of 10` & 25` under OGTT at 5 g,

single-phase LT and LT's difference of 10` under OGTT at 20 g,

bi-phase LT's and LT's differences of 5`& 25`under OGTT at 75 g,

to be specific for a healthy subject, except for human being; or

(ii) characterizing a glucose molecule in HATR-FTIR spectra by

predominant right-shifted mean peak position within 1120-1122 cm^{-1},

the highest glucose peak levels similar to glucose peak levels at 1030 - 1041 cm^{-1} over the other 2 glucose peak levels at 1080 cm^{-1} and 1153 cm^{-1},

dose-independent peak levels to high dose of glucose at 75 g under OGTT at 75 g,

cascading multi-phase LT's and LT's differences with the time intervals of 5`, 20`, 30` & 40`under OGTT at 75 g,

to be specific for a prediabetic subject, except for human being; or

(iii) characterizing a glucose molecule in HATR-FTIR spectra by

dominant right-shifted mean peak position at 1120-1122 cm^{-1},

the highest glucose peak levels within 1120-1122 cm^{-1} over glucose peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1153 cm^{-1} in HATR-FTIR spectra,

dose-dependent peak levels to low, medium and high doses of glucose at 5 g, 20 g and 75 g under OGTT at 5 g, 20 g and 75 g,

three-phase LT's and LT's differences of 0`, 10` & 25`under OGTT at 5 g,

single-phase LTs and LT's differences of 5` under OGTT at 20 g,

single-phase LT and LT's differences of 0` under OGTT at 75 g,

to be specific for a diabetic subject, except for human being.

9. A spectral method for in vivo glucose molecule characterization at 1153 cm^{-1}, characterized by spectral bounded bands at 1153 cm^{-1} in HATR-FTIR spectra corresponding to identity and structures to glucose molecules in correlation with characteristic measurements of the peak position and its shift, the peak levels measured in the interstitial fluid of the epidermal skin tissue of a healthy, prediabetic or diabetic subject, except for human being, under post-

prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g by HATR-FTIR spectroscopy, consisting one of the following:

(i) characterizing a glucose molecule in HATR-FTIR spectra by

predominant left-shifted mean peak position within 1149-1153 cm^{-1},

the lowest glucose peak levels within 1153 cm^{-1} below glucose peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1},

bi-phase LTs and LT's differences of 35`& 50`under OGTT at 5 g,

bi-phase LTs and LT's differences of 10`& 15` under OGTT at 20 g,

single-phase LT and LT's difference of 10` under OGTT at 75 g,

to be specific for a healthy subject, except for human being; or

(ii) characterizing a glucose molecule in HATR-FTIR spectra by

the lowest glucose peak levels within 1153 cm^{-1} below glucose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1},

cascading LT's and LT's differences of 0`, 15`, 25`& 55` under OGTT at 75 g,

to be specific for a prediabetic subject, except for human being; or

(iii) characterizing a glucose molecule in HATR-FTIR spectra by

predominant right-shifted mean peak position within 1153-1157 cm^{-1},

the lowest glucose peak levels within 1153 cm^{-1} below glucose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1},

bi-phase LTs and LT's differences of 15`& 25` under OGTT at 5 g,

bi-phase LTs and LT's differences of 25`& 40` under OGTT at 20 g,

single-phase LT and LT's difference of 30` under OGTT at 75 g,

to be specific for a diabetic subject, except for human being.

10. A spectral method for in vivo glucose molecule characterization of a combination group of glucose molecules with characteristic spectral parameters at consistent and significant absorption wave number at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, characterized by spectral bounded bands at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in HATR-FTIR spectra corresponding to identity and structures to glucose molecules in

correlation with characteristic measurements of the peak position and its shift, the peak levels measured in the interstitial fluid of the epidermal skin tissue of a healthy, prediabetic or diabetic subject, except for human being, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g by HATR-FTIR spectroscopy, consisting one of the following:

(i) characterizing a combination group of glucose molecules in HATR-FTIR spectra by

bi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 15` and 30` under OGTT at 5 g according to Table 2 (column 3, row 2),

single-phase LTs and LT's differences at 1030-1041 cm^{-1} of 10` under OGTT at 20 g according to Table 2 (column 4, row 2),

bi-phase LTs and LT's differences with CBG at 1030-1041 cm^{-1} of 5`and 30`under OGTT at 75 g according to Table 2 (column 5, row 2),

bi-phase LTs and LT's differences at 1080 cm^{-1} of 15` and 30` under OGTT at 5 g according to Table 2 (column 3, row 3),

three-phase LTs and LT's differences at 1080 cm^{-1} of 0`, 10`and 20` under OGTT at 20 g according to Table 2 (column 4, row 3),

single-phase LTs and LT's differences with CBG at 1080 cm^{-1} of 5`under OGTT at 75 g according to Table 2 (column 5, row 3),

bi-phase LTs and LT's differences at 1118 cm^{-1} of 10` and 25` under OGTT at 5 g according to Table 2 (column 3, row 4),

single-phase LT and LT's difference at 1118 cm^{-1} of 10` under OGTT at 20 g according to Table 2 (column 4, row 4),

bi-phase LTs and LT's differences at 1118 cm^{-1} of 5` and 25`under OGTT at 75 g according to Table 2 (column 5, row 4),

bi-phase LTs and LT's differences at 1153 cm^{-1} of 35` and 50`under OGTT at 5 g according to Table 2 (column 3, row 5),

single-phase LT and LT's difference at 1153 cm^{-1} of 10`and 15` under OGTT at 20 g according to Table 2 (column 4, row 5),

single-phase LT and LT's difference at 1153 cm^{-1} of 30` under OGTT at 75 g according to Table 3 (column 5, row 5),

the longest durations of LT's differences of

5`& 30` (75 g), 10` (20 g) and 15`& 30` (5 g) at 1030-1041 cm^{-1},

5` (75 g), 0`& 10`& 20` (20 g) and 15`& 30` (5 g) at 1080 cm^{-1},

5`& 25` (75 g), 10` (20 g) and 10`& 25` (5 g) at 1118 cm^{-1},

10` (75 g), 10` & 15` (20 g) and 35`and 50` at 1153 cm^{-1}

under OGTT with different doses according to Table 2,

dose-independent LTs and LT's differences for each assigned glucose-specific peak under any OGTT with different doses of 5 g, 20 g or 75 g,

bi-phase LTs with LT's differences of 15` & 30` at 1030-1041 cm^{-1}, 15` & 30` at 1080 cm^{-1}, 10` & 25` at 1118 cm^{-1}, 35` & 50` at 1153 cm^{-1} under OGTT at 5 g according to Table 2 (column 3),

single-, bi-phase and cascading multi-phase LTs with LT's differences of 10` at 1030-1041 cm$^{-1}$, 0` & 10` and 20` at 1080 cm^{-1}, 10`at 1118 cm$^{-1}$, 10` & 15`at 1153 cm^{-1} under OGTT at 20 g according to Table 2 (column 4),

single- and bi-phase LTs with LT's differences of 5`& 30`at 1030-1041 cm^{-1}, 5` at 1080 cm$^{-1}$, 5`& 25`at 1118 cm$^{-1}$, 10` at 1153 cm^{-1} under OGTT at 75 g according to Table 2 (column 5),

the longest durations of LT's differences starting from 5` with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a healthy subject, except for human being, according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2),

as compared with the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a diabetic subject, except for human being, according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4), and

as compared with the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a prediabetic subject according to Table 7 (column 3),

to be specific for a healthy subject, except for human being, or

(ii) characterizing a combination group of glucose molecules in HATR-FTIR spectra by

cascading multi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 5`, 20`, 30`& 45` under OGTT at 75 g according to Table 7 (column 3, row 2),

cascading multi-phase LTs and LT's differences at 1080 cm^{-1} of 5`, 20`& 45`under OGTT at 75 g according to Table 7 (column 3, row 3),

cascading multi-phase LTs and LT's differences at 1118 cm^{-1} of 5`, 20`, 30`& 40` under OGTT at 75 g according to Table 7 (column 3, row 4),

cascading multi-phase LTs and LT's differences at 1153 cm^{-1} of 0`, 15`, 25`& 55` under OGTT at 75 g according to Table 7 (column 3, row 5),

cascading multi-phase LTs and LT's differences of 5`- 45` at 1030-1041 cm^{-1}, 5`- 45` at 1080 cm^{-1}, 5`- 40` at 1118 cm^{-1}, 0`- 55` at 1153 cm^{-1} under OGTT at 75 g,

dose-independent LTs and LT's differences with cascading multi-phase appearances at

5`, 20`, 30` & 45` at 1030-1041 cm^{-1},

5`, 20` & 45` at 1080 cm^{-1},

5`, 20`, 30` & 40` at 1118 cm^{-1},

0`, 15`, 25` & 55` at 1153 cm^{-1}

under OGTT at 75 g according to Table 7 (column 3, rows 2-5),

the shortest durations of LT's differences of starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g according to Table 7 (column 3),

as compared with the shortest durations of LT's differences starting from 0`with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a diabetic subject, except for human being, according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4), and

as compared with the longest durations of LT's differences starting from 5` with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a healthy subject, except for human being, according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2),

to be specific for a prediabetic subject, except for human being; or

(iii) characterizing a combination group of glucose molecules in HATR-FTIR spectra by

bi-phase LTs and LT's differences of 0` & 10` at 1030-1041 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 2),

single-phase LT and LT's difference of 0` at 1030-1041 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 2),

single-phase LT and LT's difference of 0` at 1030-1041 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 2),

single-phase LT and LT's difference of 10` at 1080 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 3),

single-phase LT and LT's difference of 15`at 1080 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 3),

single-phase LT and LT's difference of 0`at 1080 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 3) and to Table 7 (column 4, row 3),

cascading multi-phase LTs and LT's differences of 0`, 10` & 25` at 1118 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 4),

single-phase LT and LT's difference of 5` at 1118 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 4),

single-phase LT and LT's difference of 0` at 1118 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 4),

bi-phase LTs and LT's differences of 15`& 25` under OGTT at 5 g according to Table 3 (column 3, row 5),

bi-phase LTs and LT's differences of 25`& 40` under OGTT at 20 g according to Table 3 (column 4, row 5),

single-phase LT and LT's differences of 30` under OGTT at 75 g according to Table 3 (column 5, row 5),

the shortest durations of LT's differences of

0` (75 g), 0` (20 g), 0` & 10` (5 g) at 1030-1041 cm^{-1},

0` (75 g), 15` (20 g), 10` (5 g) at 1080 cm^{-1},

0` (75 g), 5` (20 g), 0`& 10`& 25` (5 g) at 1118 cm^{-1},

30` (75 g), 25` & 40` (20 g), 15`& 25` at 1153 cm^{-1}

under OGTT with different doses according to Table 3,

the shortest durations of LTs and LT's differences of

0` at 1030-1041 cm^{-1},

0`, 0`& 60` or 60` at 1080 cm^{-1},

0` or 0`& 60` at 1118 cm^{-1},

30`& 60` at 1153 cm^{-1}

under post-prandial glucose test according to Table 1,

dose-dependent LTs and LT's differences at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} under any OGTT with different doses at 5 g, 20 g and 75 g glucose,

single-, bi-phase and cascading multi-phase LTs and LT's differences of 0` & 10` at 1030-1041 cm^{-1}, 10' at 1080 cm^{-1}, 0`, 10` & 25` at 1118 cm$^{-1}$, 15` & 25` at 1153 cm^{-1} under OGTT at 5 g according to Table 3 (column 3),

single- and bi-phase LTs and LT's differences of 0` at 1030-1041 cm^{-1}, 15' at 1080 cm^{-1}, 5' at 1118 cm^{-1}, 15'& 40' at 1153 cm^{-1} under OGTT at 20 g according to Table 3 (column 4),

single-phase LT and and LT's differences of 0' at 1030-1041 cm^{-1}, 0' at 1080 cm^{-1}, 0' at 1118 cm^{-1}, 30' at 1153 cm^{-1} under OGTT at 75 g according to Table 3 (column 5),

the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4),

as compared with the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a prediabetic subject, except for human being, according to Table 7 (column 3), and

as compared with the longest durations of LT's differences starting from 5` with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153

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cm^{-1} under OGTT at 75 g in a healthy subject, except for human being, according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2),

to be specific for a diabetic subject with type 2, except for human being.

11. The method as claimed in any of claims 6 to 10 for diagnosing disorders of glucose metabolism including prediabetes and diabetes in a subject except for human being, or for screening and following up development of diabetes in a healthy subject except for human being, or for screening and following up development of diabetes in a subject with prediabetes except for human being, or for predicting the risk of hyperglycemia in a subject except for human being, or for staging type 2 diabetes in a subject except for human being, or for managing a subject with or without hyperglycemia except for human being, or for assessing the quality of metabolic control in a subject except for human being, or for determining effective therapy in a subject with type 2 diabetes except for human being, or for determining effective dosage of drug in a subject with type 2 diabetes except for human being, or for stratifying a subject to therapeutic regimen for treating or preventing diabetes by determining prognosis of treatment in prediabetic and diabetic subject except for human being, by obtaining spectral data information comprising spectral patterns specific to healthy, prediabetes and diabetic subjects.

12. The method as claimed in any of claims 6 to 10, wherein LT is the time interval from the time-point of induction of glucose excursions till the time-point of maximum detected levels of said glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on HATR-FTIR spectrometer in the interstitial fluid of skin tissue in gathered HATR-FTIR spectra from the forearm of a tested subject under post-prandial glucose test or OGTT (oral glucose tolerance test) with different doses at 5 g, 20 g and 75 g.

13. A medicament for detecting glucose molecule species with absorption wave numbers at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy for use in a method of diagnosing prediabetes and diabetes in a subject, except for human being, under post-prandial glucose test or OGTT (oral glucose tolerance test) with different doses at 5 g, 20 g and 75 g, comprising the steps in Claim 1 or Claim 2.

14. HATR-FTIR spectroscopy for use in diagnosing disorders of glucose metabolism including prediabetes and diabetes in a subject, or for use in screening and following up

development of diabetes in a healthy subject, or for use in screening and following up development of diabetes in a subject with prediabetes, or for use in predicting the risk of hyperglycemia in a subject, or for use in staging type 2 diabetes in a subject, or for use in managing a subject with or without hyperglycemia, or for use in assessing the quality of metabolic control in a subject, or for use in determining effective therapy in a subject with type 2 diabetes, or for use in determining effective dosage of drug in a subject with type 2 diabetes, or for use in stratifying a subject to therapeutic regimen for treating or preventing diabetes by determining prognosis of treatment in prediabetic and diabetic subject, by obtaining spectral data information comprising spectral patterns specific to healthy, prediabetes and diabetic subjects, consisting of:

(i) assigning glucose-specific peaks with characteristic absorption wave numbers at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the 700-4000 cm^{-1} region in gathered HATR-FTIR spectra from the forearm of a tested subject, under post-prandial glucose test or OGTT (oral glucose tolerance test) with different doses at 5 g, 20 g and 75 g, wherein spectrally assigned glucose-specific peaks at 1030 cm^{-1} and 1041 cm^{-1} are always bounded bands together;

(ii) determining spectral characteristics of glucemic variability (GV) for each assigned glucose-specific peak in correlation with the peak position and its shift to the left or to the right in HATR-FTIR spectra, wherein shifts of the peak position at 1030 - 1041 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are characteristic for healthy, prediabetic and diabetic subjects, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g;

(iii) determining spectral characteristics of GV for each assigned glucose-specific peak in correlation with the peak level in HATR-FTIR spectra, wherein determination of the highest peak level at 1030 - 1041 cm^{-1} and determination of the highest peak level among all assigned glucose-specific peaks is characteristic for healthy, prediabetic and diabetic subjects, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g;

(iv) determining spectral characteristics of GV for each assigned glucose-specific peak in correlation with dose-dependent dynamic changes of the peak level under a continuous 120-minute test monitoring at pre-determined time-intervals from the starting till the ending time-points under comparative OGTT test with 5 g, 20 g and 75 g glucose, wherein the levels of the peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are independent to intaken dose of glucose under OGTT at 5 g (low), 20 g (medium) and 75 g (high) in healthy subjects, the

levels of the peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are dependent to intaken dose of glucose under OGTT at 5 g (low), 20 g (medium) and 75 g (high) in prediabetic and diabetic subjects**;**

(v) recognizing the spectral pattern of individual metabolic response by a continuous monitoring of GV, to be specific for healthy, prediabetic and diabetic subjects,

wherein

the spectral pattern with predominant left-shifted mean peak position towards 1030 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 8 c-e and Figure 11 a, predominant left-shifted mean peak position towards 1116-1118 cm^{-1} at 1118 cm^{-1} according to Figure 5 c and Figure 7 a, predominant left-shifted mean peak position towards 1149-1153 cm^{-1} at 1153 cm^{-1} according to Figure 8 e and Figure 11 d, highest glucose peak levels at 1030-1041 cm^{-1} over for peaks levels at 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} according to Figure 8 c-e, lowest glucose peak levels at 1153 cm^{-1} below peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 e, independent to intaken glucose dose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 5 g (low), 20 g (medium) and 75 g (high) according to Figure 5 a-c, to be specific for a healthy subject, or

the spectral pattern with predominant right-shifted mean peak position towards 1037-1041 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 8 f and Figure 11 a, predominant right-shifted mean peak position towards 1120-1122 cm^{-1} at 1118 cm^{-1} according to Figure 11 c, similarly high peak levels at 1030-1041 cm^{-1} and at 1118 cm^{-1} over for peak levels at 1080 cm^{-1} and 1153 cm^{-1} according to Figure 8 f, lowest glucose peak levels at 1153 cm^{-1} below peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 11 d, dependent to intaken glucose dose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} under OGTT at 5 g (low), 20 g (medium) and 75 g (high) according to Figure 11 a-c, to be specific for a prediabetic subject, or

the spectral pattern with dominant right-shifted mean peak position towards 1041 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 6 a, 8 a-b and 11 a, dominant right-shifted mean peak position towards 1120-1122 cm^{-1} at 1118 cm^{-1} according to Figure 6 c, dominant right-shifted mean peak position towards 1153-1157 cm^{-1} at 1153 cm^{-1} according to Figure 8 b, highest glucose peak levels at 1118 cm^{-1} over for peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1153 cm^{-1} according to Figure 8 b, lowest glucose peak levels at 1153 cm^{-1} below peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 b, dependent to intaken glucose

dose peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} under OGTT at 5 g (low), 20 g (medium) and 75 g (high) according to Figure 6 a-c, to be specific for a diabetic subject with type 2.

15. HATR-FTIR spectroscopy for use in diagnosing disorders of glucose metabolism including prediabetes and diabetes in a subject, or for use in screening and following up development of diabetes in a healthy subject, or for use in screening and following up development of diabetes in a subject with prediabetes, or for use in predicting the risk of hyperglycemia in a subject, or for use in staging type 2 diabetes in a subject, or for use in managing a subject with or without hyperglycemia, or for use in assessing the quality of metabolic control in a subject, or for use in determining effective therapy in a subject with type 2 diabetes, or for use in determining effective dosage of drug in a subject with type 2 diabetes, or for use in stratifying a subject to therapeutic regimen for treating or preventing diabetes by determining prognosis of treatment in prediabetic and diabetic subject, by obtaining spectral data information comprising spectral patterns specific to healthy, prediabetes and diabetic subjects, consisting of:

(i) assigning glucose-specific peaks with characteristic absorption wave numbers at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the 700-4000 cm^{-1} region in gathered HATR-FTIR spectra from the forearm of a tested subject, under post-prandial glucose test or OGTT with different doses at 5 g, 20 g and 75 g, wherein spectrally assigned glucose-specific peaks at 1030 cm^{-1} and 1041 cm^{-1} are always bounded bands together;

(ii) calculating the latency time (LT) duration for each assigned glucose-specific peak at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, wherein said LT is the time interval from the time-point of induction of glucose excursions till the time-point of maximum detected levels of said glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on HATR-FTIR spectrometer in the interstitial fluid of skin tissue;

(iii) comparing calculated LT duration for each assigned glucose-specific peak at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the interstitial fluid of skin tissue with the LT duration in capillary blood glucose (CBG) gathered in the same subject, by calculating the LT differences, wherein said LT is the time interval from the time-point of induction of glucose excursions till the time-point of maximum detected levels of said CBG measurements in said subject;

(iv) determining spectral characteristics for calculated LT and LT's difference intervals for each assigned glucose-specific peak in correlation with their durations, wherein the shortest and the longest intervals in minutes to be specific for healthy, prediabetic and diabetic subjects;

(v) determining spectral characteristics for calculated LT and LT's difference intervals for each assigned glucose-specific peak in correlation with their phasic appearances, wherein single, bi-phasic and cascading multi-phase appearance to be specific for healthy, prediabetic and diabetic subjects;

(vi) determining spectral characteristics for calculated LT and LT's difference intervals for each assigned glucose-specific peak in correlation with dose-dependency, to be specific for healthy, prediabetic and diabetic subjects;

(vii) determining the spectral pattern of individual metabolic response by calculating LT and LT's difference intervals for each assigned glucose-specific peak under post-prandial glucose test and OGTT with different doses at 5 g, 20 g and 75 g, to be specific for healthy, prediabetic and diabetic subjects,

wherein

the spectral pattern characterized by

bi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 15` and 30` under OGTT at 5 g according to Table 2 (column 3, row 2),

single-phase LTs and LT's differences at 1030-1041 cm^{-1} of 10` under OGTT at 20 g according to Table 2 (column 4, row 2),

bi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 5`and 30`under OGTT at 75 g according to Table 2 (column 5, row 2),

bi-phase LTs and LT's differences at 1080 cm^{-1} of 15` and 30` under OGTT at 5 g according to Table 2 (column 3, row 3),

cascading multi-phase LTs and LT's differences at 1080 cm^{-1} of 0`, 10`and 20` under OGTT at 20 g according to Table 2 (column 4, row 3),

single-phase LTs and LT's differences at 1080 cm^{-1} of 5` under OGTT at 75 g according to Table 2 (column 5, row 3),

bi-phase LTs and LT's differences at 1118 cm^{-1} of 10` and 25` under OGTT at 5 g according to Table 2 (column 3, row 4),

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single-phase LT and LT's difference at 1118 cm^{-1} of 10` under OGTT at 20 g according to Table 2 (column 4, row 4),

bi-phase LTs and LT's differences at 1118 cm^{-1} of 5` and 25` under OGTT at 75 g according to Table 2 (column 5, row 4),

bi-phase LTs and LT's differences at 1153 cm^{-1} of 35` and 50` under OGTT at 5 g according to Table 2 (column 3, row 5),

single-phase LT and LT's difference at 1153 cm^{-1} of 10`and 15` under OGTT at 20 g according to Table 2 (column 4, row 5),

single-phase LT and LT's difference at 1153 cm^{-1} of 30` under OGTT at 75 g according to Table 3 (column 5, row 5),

the longest durations of LT's differences of

5`& 30` (75 g), 10` (20 g) and 15`& 30` (5 g) at 1030-1041 cm^{-1},

5` (75 g), 0`& 10`& 20` (20 g) and 15`& 30` (5 g) at 1080 cm^{-1},

5`& 25` (75 g), 10` (20 g) and 10`& 25` (5 g) at 1118 cm^{-1},

10` (75 g), 10` & 15` (20 g) and 35`and 50` at 1153 cm^{-1}

under OGTT with different doses according to Table 2,

dose-independent LTs and LT's differences for each assigned glucose-specific peak under any OGTT with different doses of 5 g, 20 g or 75 g,

bi-phase LTs with LT's differences of 15` & 30` at 1030-1041 cm^{-1}, 15` & 30` at 1080 cm^{-1}, 10` & 25` at 1118 cm^{-1}, 35` & 50` at 1153 cm^{-1} under OGTT at 5 g according to Table 2 (column 3),

single-, bi-phase and cascading multi-phase LTs with LT's differences of 10` at 1030-1041 cm$^{-1}$, 0` & 10` and 20` at 1080 cm^{-1}, 10`at 1118 cm$^{-1}$, 10` & 15`at 1153 cm^{-1} under OGTT at 20 g according to Table 2 (column 4),

single- and bi-phase LTs with LT's differences of 5`& 30`at 1030-1041 cm^{-1}, 5` at 1080 cm$^{-1}$, 5`& 25`at 1118 cm$^{-1}$, 10` at 1153 cm^{-1} under OGTT at 75 g according to Table 2 (column 5),

the longest durations of LT's differences starting from 5`with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT

at 75 g in a healthy subject, except for human being, according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2),

as compared with the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a diabetic subject, except for human being, according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4), and

as compared with the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a prediabetic subject, except for human being, according to Table 7 (column 3),

to be specific for a healthy subject, or

the spectral pattern characterized by

cascading multi-phase LTs and LT's differences at 1030-1041 cm^{-1} of 5`, 20`, 30`& 45` under OGTT at 75 g according to Table 7 (column 3, row 2),

cascading multi-phase LTs and LT's differences at 1080 cm^{-1} of 5`, 20`& 45`under OGTT at 75 g according to Table 7 (column 3, row 3),

cascading multi-phase LTs and LT's differences at 1118 cm^{-1} of 5`, 20`, 30`& 40` under OGTT at 75 g according to Table 7 (column 3, row 4),

cascading multi-phase LTs and LT's differences at 1153 cm^{-1} of 0`, 15`, 25`& 55` under OGTT at 75 g according to Table 7 (column 3, row 5),

cascading multi-phase LTs and LT's differences of 5`- 45` at 1030-1041 cm^{-1}, 5`- 45` at 1080 cm^{-1}, 5`- 40` at 1118 cm^{-1}, 0`- 55` at 1153 cm^{-1} under OGTT at 75 g,

dose-independent LTs and LT's differences with cascading multi-phase appearances at

5`, 20`, 30` & 45` at 1030-1041 cm^{-1},

5`, 20` & 45` at 1080 cm^{-1},

5`, 20`, 30` & 40` at 1118 cm^{-1},

0`, 15`, 25` & 55` at 1153 cm^{-1}

under OGTT at 75 g according to Table 7 (column 3, rows 2-5),

the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g according to Table 7 (column 3),

as compared with the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a diabetic subject, except for human being, according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4), and

as compared with the longest durations of LT's differences starting from 5` with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a healthy subject according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2),

to be specific for a prediabetic subject, or

the spectral pattern characterized by

bi-phase LTs and LT's differences of 0` & 10` at 1030-1041 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 2),

single-phase LT and LT's difference of 0` at 1030-1041 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 2),

single-phase LT and LT's difference of 0` at 1030-1041 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 2),

single-phase LT and LT's difference of 10` at 1080 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 3),

single-phase LT and LT's difference of 15` at 1080 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 3),

single-phase LT and LT's difference of 0` at 1080 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 3) and to Table 7 (column 4, row 3),

cascading multi-phase LTs and LT's differences of 0`, 10` & 25` at 1118 cm^{-1} under OGTT at 5 g according to Table 3 (column 3, row 4),

single-phase LT and LT's difference of 5` at 1118 cm^{-1} under OGTT at 20 g according to Table 3 (column 4, row 4),

single-phase LT and LT's difference of 0` at 1118 cm^{-1} under OGTT at 75 g according to Table 3 (column 5, row 4),

bi-phase LTs and LT's differences of 15`& 25` under OGTT at 5 g according to Table 3 (column 3, row 5),

bi-phase LTs and LT's differences of 25`& 40` under OGTT at 20 g according to Table 3 (column 4, row 5),

single-phase LT and LT's differences of 30` under OGTT at 75 g according to Table 3 (column 5, row 5),

the shortest durations of LT's differences of

0` (75 g), 0` (20 g), 0` & 10` (5 g) at 1030-1041 cm^{-1},

0` (75 g), 15` (20 g), 10` (5 g) at 1080 cm^{-1},

0` (75 g), 5` (20 g), 0`& 10`& 25` (5 g) at 1118 cm^{-1},

30` (75 g), 25` & 40` (20 g), 15`& 25` at 1153 cm^{-1}

under OGTT with different doses according to Table 3,

the shortest durations of LTs and LT's differences of

0` at 1030-1041 cm^{-1},

0`, 0`& 60` or 60` at 1080 cm^{-1},

0`or 0`& 60` at 1118 cm^{-1},

30`& 60` at 1153 cm^{-1}

under post-prandial glucose test according to Table 1,

dose-dependent LTs and LT's differences at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} under any OGTT with different doses at 5 g, 20 g and 75 g glucose,

single-, bi-phase and cascading multi-phase LTs and LT's differences of 0` & 10` at 1030-1041 cm^{-1}, 10' at 1080 cm^{-1}, 0`, 10` & 25` at 1118 cm$^{-1}$, 15` & 25` at 1153 cm^{-1} under OGTT at 5 g according to Table 3 (column 3),

single- and bi-phase LTs and LT's differences of 0` at 1030-1041 cm^{-1}, 15' at 1080 cm^{-1}, 5' at 1118 cm^{-1}, 15'& 40' at 1153 cm^{-1} under OGTT at 20 g according to Table 3 (column 4),

single-phase LT and and LT's differences of 0' at 1030-1041 cm^{-1}, 0' at 1080 cm^{-1}, 0' at 1118 cm^{-1}, 30' at 1153 cm^{-1} under OGTT at 75 g according to Table 3 (column 5),

the shortest durations of LT's differences starting from 0` with single-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g according to Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4),

as compared with the shortest durations of LT's differences starting from 0` with cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a prediabetic subject, according to Table 7 (column 3), and

as compared with the longest durations of LT's differences starting from 5` with single-, bi- or cascading multi-phase appearances at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT at 75 g in a healthy subject, except for human being, according to Table 2 (column 5), Table 4 (column 2) or Table 7 (column 2),

to be specific for a diabetic subject with type 2.

Dated this 12th day of September 2014.

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PATENT AGENT [IN/PA-1740]

METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE AND FOR GENERATING PREDICTIVE CLINICAL METRICS

BACKGROUND OF THE INVENTION
FIELD OF THE INVENTION

The invention relates generally to monitoring metabolic response in a qualified subject, that comprises the step of consecutive performance of a plurality of measurements and further calculations of glucose levels, obtained by HATR-FTIR (horizontally attenuated total reflection Fourier transform infrared) spectroscopy. More particularly, the invention further relates to calculating the lag/latency time (LT) differences between measured in capillary blood the peak glucose level and by HATR-FTIR spectroscopy the peak levels of glucose values after achieved response in test subjects from the ingestion of quantified amount of pure glucose and post-prandially, allowing to assess stability of metabolic control in healthy, prediabetic and diabetic subjects. Furthermore, qualitative and quantitative interpretation of glycemic variability (GV) by using a calculation of the LT differences, based on a method of simultaneous assessment of 5 glucose-specific values by HATR-FTIR spectroscopy, helps to generate parameters, their characteristics, patterns and, thus, to establish suitable metrics for GV in the clinical practice.

DESCRIPTION OF THE RELATED ART

There are numerous published metrics to quantify different aspects of GV, but still there is no method of GV that is accepted in the clinical practice of diabetes care. Developing a new set of metrics to evaluate normal, as well as clinically relevant high and low interstitial glucose levels might open for clinicians a new way in the interpretation of the activity of glucose metabolism for diagnosis, treatment and management of the patients with diabetes mellitus and carbohydrate metabolism disorders.

The technique of using ATR-FTIR spectroscopy has been long known for non-invasive glucose measurement, but through oral mucosa. The drawbacks of such measurements included glucose contamination of the measurement site by food and a highly variable rate of saliva.

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Attempts have been made to demonstrate a proof of HATR-FTIR spectroscopy technique to detect, characterize and verify interstitial origin of glucose-specific signals at 1030, 1041, 1080, 1118 and 1153 cm^{-1} in the skin of healthy, prediabetic and diabetic subjects during OGTT (Oral Glucose Tolerance Test) and post-prandially, randomly and on mornings, i.e. fasting measurements.

Carbohydrate intolerance is one of the major criteria for a diagnosis of diabetes mellitus. OGTT employs ingested carbohydrate in a predetermined form and an amount to quantify a test subject's response to a resulting glucose challenge. However, this test is only concerned with the peak blood level of glucose, but not with the rate of change in glucose levels or the amount of time it takes for glucose levels to fluctuate from a high point to a lower point.

The medical significance of blood glucose fluctuations, i.e. frequency and magnitude, has been a controversial topic and the subject of extensive research, proving that GV can be used to describe a general risk of hyperglycemia over long periods of time, or when focused on events of short duration, such as meals or overnight.

Since glucose on the surface of the skin and within the stratum corneum has been considered as a source for extraneous glucose contamination during testing of invasive glucose monitoring devices, there was not found any direct method for in vivo glucose molecule(s) characterization and monitoring directly on healthy, prediabetes and diabetes subjects.

SUMMARY OF THE INVENTION

An object of the present invention is to provide the user with in vivo method for monitoring individual metabolic response and for qualitative and quantitative characterization of GV, in order to further recognize patterns from the patients data for establishing predictive clinical metrics.

Specifically, the invented method is based on calculating the LT differences between the LT measured for the peak of CBG and the LT for the peaks of epidermally measured interstitial glucose levels by HATR-FTIR spectroscopy on healthy, prediabetic and diabetic subjects under OGTT with different doses (low, medium, high) and post-prandially, applicable for staging Type 2 diabetes and assessing diabetes control, including estimation of intra-day and intra-week risks, as well a general risk of hyperglycemia. More, the method can be further applied

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for screening of disorders of glucose metabolism, such as impaired glucose tolerance and diabetes mellitus by means of evaluation of the time required for glucose to diffuse from the capillary to the living skin tissue. In addition, method can be also served for individual calibration of obtained glucose profiles by HATR-FTIR spectroscopy in a dynamic time-dependent manner in a qualified subject.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 schematically presents a method for calculation of the LT differences between the LT for the peak of CBG and for the peak of each epidermally measured interstitial glucose level at 1030, 1041, 1080, 1118 and 1153 cm^{-1} by HATR-FTIR spectroscopy in a qualified subject.

Figure 2 A-D presents differences between GV obtained between CBG values (shown by dashed lines) and each glucose value (shown by solid lines) at 1030, 1041, 1118 and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 1 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Figure 3 A-D presents differences between GV obtained between CBG values (shown by dashed lines) and each glucose value (shown by solid lines) at 1030, 1041, 1118 and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 2 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Figure 4 A-D presents differences between GV obtained between CBG values (shown by dashed lines) and each glucose value (shown by solid lines) at 1030, 1041, 1118 and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 3 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Figure 5 A-C presents a comparative dose-dependent GV during monitoring of metabolic response by HATR-FTIR spectroscopy at 1030, 1041, 1118 and 1153

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cm^{-1} during OGTT at different doses, at 5 g (low), 20 g (medium) and 75 g (high), in a healthy subject (Subject 4).

Figure 6 A-C presents a comparative dose-dependent GV during monitoring of metabolic response by HATR-FTIR spectroscopy simultaneously shown at 1030, 1041, 1118 and 1153 cm^{-1} during OGTT at different doses, at 5 g (low), 20 g (medium) and 75 g (high), in Subject 3 with Type 2 diabetes.

Figure 7 A-C illustrates examples of characteristic differences in the levels of glucose values and wavenumber shifts between a healthy subject (Subject 4) and a subject with Type 2 diabetes (Subject 3) under OGTT with different doses.

Figure 8 A-F illustrates a variety of examples of GV simultaneously shown at 1030, 1041, 1118 and 1153 cm^{-1} by HATR-FTIR spectroscopy in 2 Type 2 diabetes (Fig. 8 A, B) under OGTT with 75 g and 20 g; in a prediabetic subject (Fig. 8 F) under OGTT with 75 g and under OGTT with 75 g in 3 healthy subjects (Fig. 8 C, D, E).

Figure 9 A-D presents GV simultaneously shown at 1030, 1041, 1118 and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in 3 patients (Subjects 1-3) with Type 2 diabetes, in comparison to a healthy subject (Subject 5).

Figure 10 A-C presents day-to-day variations on GV during a 120-minute post-prandial monitoring of individual metabolic response in Subject 3 with Type 2 diabetes on 2 consecutive days, comparatively shown at 1030, 1041, 1080 and 1118 cm^{-1} by HATR-FTIR spectroscopy.

Figure 11 A-D comparatively presents GV during monitoring of individual metabolic response in 3 healthy subjects (Subjects 1, 2, 4), in 1 subject as a suspect of having impaired glucose tolerance, i.e. prediabetes (Subject 3), and in Subject 3 with Type 2 diabetes by HATR-FTIR spectroscopy.

BRIEF DESCRIPTION OF THE TABLES

Table 1. LT differences estimated within a 120-minute post-prandial monitoring of metabolic response in 3 subjects with Type 2 diabetes (S1, S2 and S3) by HATR-FTIR spectroscopy.

Table 2. LT differences between the LT for the peak of CBG and the LT peak for each measured glucose level at 1030, 1041, 1080, 1118 and 1153 cm^{-1}, obtained in a healthy subject during OGTT at different doses (5 g, 20 g, 75 g).

Table 3. LT differences between the LT for the peak of CBG and the LT peak for

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each measured glucose level at 1030, 1041, 1080, 1118 and 1153 cm^{-1}, obtained in a diabetic subject during OGTT at different doses (5 g, 20 g, 75 g).

Table 4. LT differences under OGTT with 75 g., i.e. clinical, a healthy subject vs. a subject with Type 2 diabetes.

Table 5. LT differences under OGTT with 20 g., i.e. clinical, a healthy subject vs. a subject with Type 2 diabetes.

Table 6. LT differences estimated for the same subject with Type 2 diabetes on 2 consecutive days.

Table 7. OGTT (75 g)., i.e. clinical OGTT, demonstrate estimated LT differences for healthy, prediabetic and diabetic subjects.

DETAILED DESCRIPTION OF THE EMBODIMENT

As described further herein, in vivo glucose spectral measurements from the skin surface of the inner wrists of measured subjects have been performed on a commercially available FT-IR spectrometer (Shimadzu IRPrestige - 21/8400S, Japan), that measures the absorbance spectra in the 700-4000 cm^{-1} region at a resolution of 4 cm^{-1}, using 20 frames of accumulation to collect interferogram. Non-invasive glucose monitoring is achieved by tight contact of the measured site with a specially designed flat-plated prism with a mounted ATR crystal for the PIKE Technologies Horizontal accessory (ATR-8200 HA). This horizontal accessory is of a trapezoid shape with carefully chosen dimentions by a manufacturer (80 x 10 x 4 cm), in order to maximize S/N ratio in the measured spectra.

A portable glucosemeter (SKK GluTestS, Sanwa Chemical Institute, Nagoya, Japan) has been used for CBG determinations in mg/dL.

Noninvasive spectroscopic interstitial glucose monitor to an individual necessitates a calibration. Generating such a calibration requires reference CBG values that are uncorrelated to sampling factors. The invented formula provides a method to calibrate dynamic measurements of interstitial glucose values in vivo by HATR-FTIR spectroscopy, based on referenced CBG values, that are described in Figure 1.

A test subject's CBG values are controlled or manipulated through the oral ingestion of carbohydrate, i.e. meals, and/or through oral consumption of dissolved in water pure glucose at different determined doses (f.e. 5 g, 20 g, 75 g) in such a way that the changes of the targeted glucose profiles of Figures 1-4 are reproduced

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by the subject's own glucose profiles. Thus, since the subject's CBG is under active control, the influence of other sampling factors are eliminated.

Steps of the invented formula and method:

* performing reference CBG measurements at pre-determined intervals prior to spectral acquisition by HATR-FTIR spectroscopy

* gathering *in vivo* HATR-FTIR spectra from the forearm of a tested subject at predetermined intervals in the 700-4000 cm^{-1} region with further spectra normalization to amide I, at 1650 cm^{-1}, always after a background scan collection by HATR-FTIR spectroscopy

* multiple baseline correction of the 1000-1180 cm^{-1} region with assignment of glucose-specific peaks at 1030, 1041, 1080, 1118 and 1153 cm^{-1}, where the peaks at about 1030 cm^{-1} and 1041 cm^{-1} are always bounded together

* subject's forearm repositioning after each measured spectrum for avoidance of hydration effect

* manipulating a subject's capillary blood glucose levels in order to obtain meaningful time-dependent LT's and their differences by subject himself/herself under OGTT with different doses (5 g, 20 g, 75 g), post-prandially, or under any other screening metabolic test

* manipulating a subject's glucose values by HATR-FTIR such those produce meaningful time-dependent changes in the levels of CBG and in the levels of glucose values at 1030, 1041, 1080, 1118 and 1153 cm^{-1} by subject himself/herself under OGTT with different doses (5 g, 20 g, 75 g), post-prandially, or under any other screening metabolic test

* calculation of the LT differences between the estimated LT for the peak of CBG and the estimated LT for the peaks of each glucose value at 1030, 1041, 1080, 1118 and 1153 cm^{-1} measured by HATR-FTIR spectroscopy

The invention utilizes the targeted glucose profiles by HATR-FTIR spectroscopy schematically presented in Figure 1. "0"- point is pre-prandial, i.e. fasting, and/or before OGTT.

The CBG values and the spectral measurements furnish a data set upon which a calculation of the LT differences is made by using Equation 1, and which a calibration is also based in a qualified subject.

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Equation 1 utilizes only parameters described in Figure 1:

LT changes = LT (CBG peak level) − LT (HATR-FTIR peak level(s) (1030/1041/1080/1118/1153 cm⁻¹)

The various aspects of the invention are described in greater detail below.

Examples of inducing levels fluctuations/shifts in the subject's CBG values and epidermal glucose values by HATR-FTIR, in order to obtain meaningful time-dependent and dose-dependent glucose values, their LT's for maximum peaks and their LT differences towards monitored characterization of GV in a qualified subject, with or without hyperglycemia, stable or unstable, that can be used to predict the patient's risk of hyperglycemia, to stage Type II diabetes and, in general, to be considered as a new metrics of assessing the quality of metabolic control, are presented in Tables 1-5 and in Figures 2-6.

SUBJECTS

Type 2 diabetes (totally 3 subjects):

Subject 1, Male, age 67, insulin therapy because of recurrent/persistent hyperglycemia, due to no response to orally prescribed tabletes of Metformin for the last 7 years

Subject 2, Female, age 70, orally prescribed tabletes of Metformin has been changed to a diet control

Subject 3, Male, age 69, insulin therapy because of recurrent/persistent hyperglycemia, due to no response to orally prescribed tabletes of Metformin for the last 2 years

Impaired glucose tolerance, i.e. prediabetic subjects, and subjects as suspects of having impaired glucose tolerance due to occasional post-prandial hyperglycemia, based on accepted in the clinical practice interpretation of blood glucose units obtained under different conditions (mg/dL) and according to WHO Diabetes Criteria (totally 3 subjects):

Subject 1, Male, age 49, occasional post-prandial hyperglycemia

Subject 2, Male, age 58, occasional post-prandial hyperglycemia

Subject 3, Male, age 49, prediabetes

Healthy (totally 5 subjects):

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Subject 1, Male, age 23

Subject 2, Male, age 24

Subject 3, Male, age 60

Subject 4, Female, age 35

Subject 5, Male, age 59

RESULTS

1. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE IN A QUALIFIED SUBJECT

(i) individually at each glucose molecule peak value

(ii) simultaneously at all glucose molecule peak values

2. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE IN A QUALIFIED SUBJECT

(i) in one subject

(ii) between the subjects

3. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE IN A QUALIFIED SUBJECT

(i) within one group of disease/condition

(ii) between different groups/conditions

4. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE IN A QUALIFIED SUBJECT

(i) under one screening test

(ii) comparatively, under different screening tests

5. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE IN A QUALIFIED SUBJECT

(i) for qualitative interpretation

(ii) for quantitative interpretation

6. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE AND

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FOR GENERATING PREDICTIVE CLINICAL METRICS IN A PATIENT

(i) for generating a pattern and parameters characterizing GV in the patients with Type 2 diabetes

(ii) for generating a pattern and parameters characterizing GV in the patients with impaired glucose tolerance, i.e. the patients with prediabetes

(iii) for generating a pattern and parameters characterizing GV in healthy subjects

Tables 1-5 describe that:

the LT differences show dose-dependency in healthy, prediabetic and diabetic subjects, that differ at duration;

the LT differences are the shortest in a diabetes subject and the longest in a healthy subject, independent of intaken dose of glucose under OGTT;

the LT differences differ at single, bi-phasic and a cascading multi-phase appearance between healthy subjects, subjects as suspects of having impaired glucose tolerance, i.e. prediabetes, and subjects with Type 2 diabetes;

the LT differences show pattern recognition for healthy subjects, prediabetic subjects and subjects with Type 2 diabetes, based on the assessed LT changes (in minutes);

the LT differences show day-to-day variations, connected to a pattern recognition.

Figures 2-11, in addition to the results, shown in Tables 1-7, show differences in GV between healthy, prediabetic and diabetic subjects towards their pattern recognition, based on specific characteristics:

recognized to healthy and prediabetic/diabetic subjects wavenumber changes, i.e. shifts of glucose-specific peaks to the left or to the right, accordingly;

recognized glucose levels as low, medium and high, for healthy, prediabetic and diabetic subjects, assessed at determined time intervals under OGTT with different doses;

recognized meaningful time-dependent fluctuations of GV assessed at each glucose-specific peak value, having common and specific features for healthy, prediabetic and diabetic subjects;

EXAMPLES

EXAMPLE 1

DIABETIC SUBJECT / POST-PRANDIAL GLUCOSE TEST

Figure 2 a-d presents GV, the LT for each glucose molecule peak value (shown by solid lines) at 1030, 1041, 1080, 1118 and 1153 cm^{-1} and CBG values (shown by dashed lines), their LTs difference by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 1 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Figure 3 a-d presents GV, the LT for each glucose molecule peak value (shown by solid lines) at 1030, 1041, 1080, 1118 and 1153 cm^{-1} and CBG values (shown by dashed lines), their LTs difference by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 2 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Figure 4 a-d presents GV, the LT for each glucose molecule peak value (shown by solid lines) at 1030, 1041, 1080, 1118 and 1153 cm^{-1} and CBG values (shown by dashed lines), their LTs difference by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 3 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Table 1 displays LT differences estimated within a 120-minute post-prandial monitoring of metabolic response in 3 subjects with Type 2 diabetes (S1, S2 and S3) by HATR-FTIR spectroscopy.

Subjects	1030-1041 cm^{-1}	1080 cm^{-1}	1118 cm^{-1}	1153 cm^{-1}
S1	0'	0'	0'	30'

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S2	0'	0' & 60'	0' & 60'	30'
S3	0'	60'	0' ·	60'

EXAMPLE 2

HEALTHY SUBJECT / OGTT (5 g, 20 g, 75 g)

Figure 5 a-c presents a comparative dose-dependent GV during a continuous monitoring of metabolic response by HATR-FTIR spectroscopy at 1030, 1041, 1080, 1118 and 1153 cm^{-1} under OGTT with different doses, at 5 g (low), 20 g (medium) and 75 g (high), in a healthy subject (Subject 4).

Table 2 displays LT differences between the LT for the peak of CBG and the LT peak for each measured glucose molecule peak level at 1030, 1041, 1080, 1118 and 1153 cm^{-1}, obtained in a healthy subject during OGTT at different doses (5 g, 20 g, 75 g).

Healthy	LT	OGTT (5 g)	OGTT (20 g)	OGTT (75 g)
1030-1041 cm^{-1}	LT$_{differences}$	15' & 30'	10'	5' & 30'
1080 cm^{-1}	LT$_{differences}$	15' & 30'	0' & 10' & 20'	5'
1118 cm^{-1}	LT$_{differences}$	10' & 25'	10'	5 '& 25'
1153 cm^{-1}	LT$_{differences}$	35' & 50'	10' & 15'	10'

Figure 6 a-c presents a comparative dose-dependent GV during a continuous monitoring of metabolic response by HATR-FTIR spectroscopy simultaneously shown at 1030, 1041, 1080, 1118 and 1153 cm^{-1} under OGTT with different doses,

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at 5 g (low), 20 g (medium) and 75 g (high), in Subject 3 with Type 2 diabetes.

Table 3 displays LT differences between the LT for the peak of CBG and the LT peak for each measured glucose level at 1030, 1041, 1080, 1118 and 1153 cm^{-1}, obtained in a diabetic subject during OGTT at different doses (5 g, 20 g, 75 g).

Type 2 diabetes	LT	OGTT (5 g)	OGTT (20 g)	OGTT (75 g)
1030-1041 cm^{-1}	LT$_{differences}$	0' & 10'	0'	0'
1080 cm^{-1}	LT$_{differences}$	10'	15'	0'
1118 cm^{-1}	LT$_{differences}$	0' & 10 & 25'	5'	0'
1153 cm^{-1}	LT$_{differences}$	15' & 25'	25' & 40'	30'

EXAMPLE 3

DIABETIC SUBJECT vs HEALTHY SUBJECT / OGTT (5 g, 20 g, 75 g)

Figure 7 a-c illustrates examples of characteristic differences in the levels of glucose values and wavenumber shifts between a healthy subject (Subject 4) and a subject with Type 2 diabetes (Subject 3) under OGTT with different doses.

Table 4 displays LT differences under OGTT with 75 g, i.e. clinical, a healthy subject vs. a subject with Type 2 diabetes.

Subjects	healthy	Type 2 diabetes
1030-1041 cm^{-1}	15' & 30'	10'
1080 cm^{-1}	15' & 30'	10'
1118 cm^{-1}	10' & 25'	0' & 10' & 25'

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| 1153 cm^{-1} | 35' & 50' | 15' & 25' |

Table 5 displays LT differences under OGTT with 20 g, a healthy subject vs. a subject with Type 2 diabetes.

Subjects	healthy	Type 2 diabetes
1030-1041 cm^{-1}	10'	0'
1080 cm^{-1}	0' & 10' & 20'	15'
1118 cm^{-1}	10'	5'
1153 cm^{-1}	10' & 15'	25' & 40'

EXAMPLE 4

DIABETIC SUBJECT vs. PREDIABETIC SUBJECT vs. HEALTHY
SUBJECT/OGTT (20 g, 75 g)

Figure 8 a-f illustrates a variety of examples of monitored GV simultaneously shown at 1030, 1041, 1080, 1118 and 1153 cm^{-1} by HATR-FTIR spectroscopy in Type 2 diabetes (Subject 3) under OGTT with 75 g and 20 g, in a prediabetic subject (Subject 5) under OGTT with 75 g, and under OGTT with 75 g in 3 healthy subjects (Subject 1, Subject 3, Subject 4).

EXAMPLE 5

DIABETIC SUBJECT vs. HEALTHY SUBJECT/ POST-PRANDIAL GLUCOSE
TEST

Figure 9 a-d presents GV simultaneously shown at 1030, 1041, 1080, 1118 and

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1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in 3 patients (Subjects 1-3) with Type 2 diabetes, in comparison to a healthy subject (Subject 5). A 120-minute post-prandial monitoring of metabolic response in 3 subjects (S1, S2, and S3) with Type 2 diabetes and 1 healthy control subject ("0"-point is pre-prandial). CBG levels in mg/dL are shown in numbers along curves for each measured subject.

EXAMPLE 6

DIABETIC SUBJECT / POST-PRANDIAL GLUCOSE TEST / DAY-TO-DAY VARIATIONS

Fig. 10 a-c presents day-to-day variations on GV during a 120-minute post-prandial monitoring of individual metabolic response in Subject 3 with Type 2 diabetes on 2 consecutive days, comparatively shown at 1030, 1041, 1080 and 1118 cm^{-1} by HATR-FTIR spectroscopy.

Table 6 displays LT differences estimated for the same subject with Type 2 diabetes on 2 consecutive days.

Subjects	1030-1041 cm^{-1}	1080 cm^{-1}	1118 cm^{-1}	1153 cm^{-1}
S3 (Day 1)	0'	60'	0'	60'
S3 (Day 2)	0'	0'	60'	-

EXAMPLE 7

OGTT (75 g)

Figure 11 a-d comparatively presents GV during a continuous monitoring of individual metabolic response in 3 healthy subjects (Subjects 1, 2, 4), in 1 subject as a suspect of having impaired glucose tolerance, i.e. prediabetes (Subject 3),

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and in Subject 3 with Type 2 diabetes by HATR-FTIR spectroscopy under OGTT (75 g) for each glucose molecule peak at 1030-1041, 1080, 1118 and 1153 cm^{-1}.

Table 7 displays OGTT (75 g), i.e. clinical OGTT, demonstrate estimated LT differences for healthy, prediabetic and diabetic subjects.

Subjects	healthy	prediabetes	Type 2 diabetes
1030-1041 cm^{-1}	5' & 30'	5' & 20' & 30' & 45'	0'
1080 cm^{-1}	5'	5' & 20' & 45'	0'
1118 cm^{-1}	5' & 25'	5' & 20' & 30' & 40'	0'
1153 cm^{-1}	10'	0' & 15' & 25' & 55'	30'

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I claim: E-101 9535 2018

1. A method for spectral patterned data analyzing to evaluate individual metabolic response and generate predictive clinical metrics for disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for human beings by HATR-FTIR spectroscopy, comprising of:

(i) assigning glucose-specific peaks with characteristic absorption wave numbers at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the 700-4000 cm^{-1} region of a subject under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g (low, medium and/or high), wherein assigned peaks at 1030 cm^{-1} and 1041 cm^{-1} are always bounded bands in the mid-IR spectra on HATR-FTIR spectrometer;

(ii) determining characteristic spectral parameters for assigned glucose-specific peaks in correlation with each assigned peak position and/or its shift in the mid-IR spectra, wherein characteristic peak position within 1030 - 1041 cm^{-1}, characteristic shifts of the peaks at 1118 cm^{-1} and at 1153 cm^{-1} are to be specific for healthy, prediabetic and diabetic subjects under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g;

(iii) further determining characteristic spectral parameters for assigned glucose-specific peaks in correlation with each assigned peak level in the mid-IR spectra, wherein characteristic determination of the highest peak level within 1030 - 1041 cm^{-1} and characteristic determination of the highest peak level among 5 assigned glucose-specific peaks are to be specific for healthy, prediabetic and diabetic subjects under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g;

(iv) further determining characteristic spectral parameters for assigned glucose-specific peaks in correlation with dynamic changes of

each assigned peak levels to dose-response to 5 g, 20 g and 75 g glucose under comparative OGTT test with low, medium and high glucose under a continuous 120-minute monitoring at pre-determined time-intervals from the starting till the ending time-points during the test, wherein the levels of the peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are dose-indifferentiated in healthy subjects, the levels of the peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} are dose-differentiated between low, medium and high doses in prediabetic and diabetic subjects;

(v) determining the spectral pattern of individual metabolic response by a continuous monitoring of glycemic variability (GV) under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g in correlation with characteristic spectral parameters for assigned glucose-specific peaks at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and/or 1153 cm^{-1} identified in steps (ii)-(iv), to be specific for healthy, prediabetic and diabetic subjects, wherein

the spectral pattern with characteristic predominant mean peak position at 1030 cm^{-1} within 1030 - 1041 cm^{-1} according to Figure 8 c-e and Figure 11 a, predominant left-shifted mean peak position within 1116-1118 cm^{-1} according to Figure 5 c and Figure 7 a, predominant left-shifted mean peak position within 1149-1153 cm^{-1} according to Figure 8 e and Figure 11 d, the highest glucose peak levels within 1030-1041 cm^{-1} over the other 3 glucose peak levels according to Figure 8 c-e, the lowest glucose peak levels within 1153 cm^{-1} below the other 4 glucose peaks levels at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 e, indifferentiated to dose-response peak levels at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and/or 1153 cm^{-1} according to Figure 5 a-c, to be specific for a healthy subject, or

the spectral pattern with characteristic predominant mean peak position within 1037-1041 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 8f and Figure 11a, predominant right-shifted mean peak position within 1120-

1122 cm^{-1} according to Figure 11 c, the highest peak levels within 1030-1041 cm^{-1} and within 1118 cm^{-1} at similar levels over the other 2 glucose peak levels according to Figure 8 f, the lowest glucose peak levels within 1153 cm^{-1} below the other 4 glucose peaks levels at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 11d, differentiated high dose-response peak levels with 75 g at 1030 cm^{-1},1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1}, to be specific for a prediabetic subject, or

the spectral pattern with characteristic predominant mean peak position within 1041 cm^{-1} at 1030 - 1041 cm^{-1} according to Figure 6a, 8 a-b and 11a, dominant right-shifted mean peak position within 1120-1122 cm^{-1} according to Figure 6c, predominant right-shifted mean peak position within 1153-1157 cm^{-1} according to Figure 8b, the highest glucose peak levels at 1118 cm^{-1} over the other 3 glucose peak levels according to Figure 8 a-b, the lowest glucose peak levels within 1153 cm^{-1} below the other glucose peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8f and Figure 11d, differentiated low, medium and high dose-response peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and/or 1118 cm^{-1} according to Figure 6 a-c, to be specific for a diabetic subject with Type 2;

(vi) calculating the latency time (LT) for each assigned glucose-specific peak at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and/or 1153 cm^{-1}, wherein said LT is the time interval from the time-point of induction of glucose excursions in the interstitial fluid of skin tissue till the time-point of maximum detected levels of said glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on HATR-FTIR spectrometer;

(vii) calculating the LT in reference capillary blood glucose (CBG) gathered in the same subject, wherein said LT is the time interval from the time-point of induction of glucose excursions in the blood glucose till the time-point of maximum detected levels of said CBG measurements in said subject;

(viii) calculating the LT differences with CBG between the estimated LT for each glucose-specific peak measurement at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on the HATR-FTIR spectrometer;

(ix) determining characteristic spectral parameters for measured LT and calculated LT differences with CBG for each assigned glucose-specific peak in correlation with their duration, dose-dependency, phasic appearance, to be specific for healthy, prediabetic and diabetic subjects; and

(x) determining the spectral pattern of individual metabolic response by measuring the LT and the LT difference with CBG for each assigned glucose-specific peak under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g in correlation with characteristic spectral parameters identified in step (ix), to be specific for healthy, prediabetic and diabetic subjects, wherein

the spectral pattern with

characteristic bi-phase LTs and the LTs differences with CBG at 1030-1041 cm^{-1} with the time intervals of 15 minutes and 30 minutes under OGTT (5 g) with reference to Table 2 (column 3, row 2),

characteristic single-phase LTs and the LTs differences with CBG at 1030-1041 cm^{-1} with the time intervals of 10 minutes under OGTT (20 g) with reference to Table 2 (column 4, row 2),

characteristic bi-phase LTs and the LTs differences with CBG at 1030-1041 cm^{-1} with the time intervals of 5 minutes and 30 minutes under OGTT (75 g) with reference to Table 2 (column 5, row 2),

characteristic bi-phase LTs and the LTs differences with CBG at 1080 cm^{-1} with the time intervals of 15 minutes and 30 minutes under OGTT (5 g) with reference to Table 2 (column 3, row 3),

characteristic three-phase LTs and the LTs differences with CBG at 1080 cm^{-1} with the time intervals of 0 minutes, 10 minutes and 20 minutes under OGTT (20 g) with reference to Table 2 (column 4, row 3),

characteristic single-phase LTs and the LTs differences with CBG at 1080 cm^{-1} with the time intervals of 5 minutes under OGTT (75 g) with reference to Table 2 (column 5, row 3),

characteristic bi-phase LTs and the LTs differences with CBG at 1118 cm^{-1} with the time intervals of 10 minutes and 25 minutes under OGTT (5 g) with reference to Table 2 (column 3, row 4),

characteristic single-phase LTs and the LTs differences with CBG at 1118 cm^{-1} with the time intervals of 10 minutes under OGTT (20 g) with reference to Table 2 (column 4, row 4),

characteristic bi-phase LTs and the LTs differences with CBG at 1118 cm^{-1} with the time intervals of 5 minutes and 25 minutes under OGTT (75 g) with reference to Table 2 (column 5, row 4),

characteristic bi-phase LTs and the LTs differences with CBG at 1153 cm^{-1} with the time intervals of 35 minutes and 50 minutes under OGTT (5 g) with reference to Table 2 (column 3, row 5),

characteristic single-phase LTs and the LTs differences with CBG at 1153 cm^{-1} with the time intervals of 10 minutes and 15 minutes under OGTT (20 g) with reference to Table 2 (column 4, row 5),

characteristic single-phase LTs and the LTs differences with CBG at 1153 cm^{-1} with the time intervals of 10 minutes under OGTT (75 g) with reference to Table 3 (column 5, row 5),

characteristic the longest LT's differences with CBG at 1030-1041 cm^{-1} within 5-30 minutes, at 1080 cm^{-1} within 0-30 minutes, at 1118 cm^{-1} within 5-25 minutes, at 1153 cm^{-1} within 10-50 minutes under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g,

characteristic longest intervals within 5-50 minutes of the LT's differences with CBG with characteristic single-, bi- and three-phase appearance at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under

OGTT with 75 g, as compared with characteristic LT shortest durations within 0-30 minutes of the LT's differences with CBG with characteristic single-phase appearance at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on HATR-FTIR spectrometer under OGTT with 75 g for a diabetic subject as shown in Table 3 (column 5), Table 4 (column 3) and/or Table 7 (column 4) and characteristic durations of the LTs differences with CBG within 0-55 minutes with characteristic multi-phase cascade appearance at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on HATR-FTIR spectrometer under OGTT with 75 g,

characteristic dose-independent durations of the LT's and the LT's differences with CBG for each assigned glucose-specific peak under any OGTT with different doses of 5 g, 20 g and 75 g,

characteristic bi-phase LT's appearance with calculated LT's differences of 15 minutes and 30 minutes at 1030-1041 cm^{-1}, 15 minutes and 30 minutes at 1080 cm^{-1}, 10 minutes and 25 minutes at 1118 cm^{-1}, 35 minutes and 50 minutes at about 1153 cm^{-1} under OGTT (5 g) with reference to Table 2 (column 3),

characteristic single-, bi- and three-phase LT's appearance with calculated LT's differences of 10 minutes at 1030-1041 cm^{-1}, 0 minutes and 10 minutes and 20 minutes at 1080 cm^{-1}, 10 minutes at 1118 cm^{-1}, 10 minutes and 15 minutes at 1153 cm^{-1} under OGTT (20 g) with reference to Table 2 (column 4),

characteristic single- and bi-phase LT's appearance with calculated LT's differences of 5 minutes & 30 minutes at 1030-1041 cm^{-1}, 5 minutes at 1080 cm^{-1}, 5 minutes & 25 minutes at 1118 cm^{-1}, 10 minutes at 1153 cm^{-1} under OGTT (75 g) with reference to Table 2 (column 5),
to be specific for a healthy subject, or

the spectral pattern with

characteristic multi-phase LTs and the LTs differences with CBG at 1030-1041 cm^{-1} with the time intervals of 5, 20, 30 and 45 minutes under OGTT (75 g) with reference to Table 7 (column 3, row 2),

characteristic three-phase LTs and the LTs differences with CBG at 1080 cm^{-1}, with the time intervals of 5, 20 and 45 minutes under OGTT (75 g) with reference to Table 7 (column 3, row 3),

characteristic cascading multi-phase LTs and the LTs differences with CBG at 1118 cm^{-1} with the time intervals of 5, 20, 30 and 40 minutes under OGTT (75 g) with reference to Table 7 (column 3, row 4),

characteristic cascading multi-phase LTs and the LTs differences with CBG at 1153 cm^{-1} with the time intervals of 0, 15, 25 and 55 minutes under OGTT (75 g) with reference to Table 7 (column 3, row 5),

characteristic multi-phase LTs and the LTs differences with CBG within 5- 45 minutes at 1030-1041 cm^{-1}, 5- 45 minutes at 1080 cm^{-1}, 5- 40 minutes at 1118 cm^{-1}, 0- 55 minutes at 1153 cm^{-1} under OGTT with 75 g as shown in Table 7 (column 3, rows 2-5),

characteristic LTs differences with CBG within 0-55 minutes with characteristic multi-phase cascade appearance at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on HATR-FTIR spectrometer under OGTT with 75 g, as compared with characteristic shortest intervals within 0-30 minutes of the LT's differences with CBG with characteristic single-phase appearance at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on HATR-FTIR spectrometer under OGTT with 75 g for a diabetic subject as shown in Table 3 (column 5), Table 4 (column 3) and Table 7 (column 4) and with characteristic longest intervals within 5-50 minutes of the LT's differences with CBG with characteristic single-, bi- and three-phase appearance at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT with 75 g for a healthy subject as shown in Table 2 (column 5),

characteristic dose-dependent durations of the LT's and the LT's differences with CBG with multi-phase cascade appearance of 5, 20, 30 and 45 minutes at 1030-1041 cm^{-1}, at 5, 20 and 45 minutes at 1080 cm^{-1}, at 5, 20, 30 and 40 minutes at 1118 cm^{-1}, at 0, 15, 25 and 55 minutes at 1153 cm^{-1} under OGTT with 75 g, · to be specific for a prediabetic subject, or

the spectral pattern with

characteristic bi-phase LTs and the LTs differences with CBG at 1030-1041 cm^{-1} with the time intervals of 0 minutes and 10 minutes under OGTT (5 g) with reference to Table 3 (column 3, row 2),

characteristic single-phase LTs and the LTs differences with CBG at 1030-1041 cm^{-1} with the time intervals of 0 minutes under OGTT (20 g) with reference to Table 3 (column 4, row 2),

characteristic single-phase LTs and the LTs differences with CBG at 1030-1041 cm^{-1} with the time intervals of 0 minutes under OGTT (75 g) with reference to Table 3 (column 5, row 2),

characteristic single-phase LTs and the LTs differences with CBG at 1080 cm^{-1} with the time interval of 10 minutes under OGTT (5 g) with reference to Table 3 (column 3, row 3),

characteristic single-phase LTs and the LTs differences with CBG at 1080 cm^{-1} with the time interval of 15 minutes under OGTT (20 g) with reference to Table 3 (column 4, row 3),

characteristic single-phase LTs and the LTs differences with CBG at 1080 cm^{-1} with the time interval of 0 minutes under OGTT (75 g) with reference to Table 3 (column 5, row 3) and to Table 7 (column 4, row 3),

characteristic three-phase LTs and the LTs differences with CBG at 1118 cm^{-1} with the time intervals of 0 minutes, 10 minutes and 25 minutes under OGTT (5 g) with reference to Table 3 (column 3, row 4),

characteristic single-phase LTs and the LTs differences with CBG at 1118 cm^{-1} with the time intervals of 5 minutes under OGTT (20 g) with reference to Table 3 (column 4, row 4),

characteristic single-phase LTs and the LTs differences with CBG at 1118 cm^{-1} with the time intervals of 0 minutes under OGTT (75 g) with reference to Table 3 (column 5, row 4),

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 15 minutes and 25 minutes under OGTT (5 g) with reference to Table 3 (column 3, row 5),

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 25 minutes and 40 minutes under OGTT (20 g) with reference to Table 3 (column 4, row 5),

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 30 minutes under OGTT (75 g) with reference to Table 3 (column 5, row 5),

characteristic the shortest LTs differences at 1030-1041 cm^{-1} of 0 minutes and 10 minutes, at 1080 cm^{-1} of 0, 10, 15 and 60 minutes, at 1118 cm^{-1} of 0, 5, 10, 25 and 60 minutes, at 1153 cm^{-1} of 15, 25, 30 and 40 minutes under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g,

characteristic shortest LTs within the shortest intervals of the LTs differences at 1030-1041 cm^{-1} of 0 minutes as shown in Table 1 (column 2), at 1080 cm^{-1} of 0, 0`& 60 and 60 minutes as shown in Table 1 (column 3), at 1118 cm^{-1} of 0 and 0 & 60 minutes as shown in Table 1 (column 4), at 1153 cm^{-1} of 30 and 60 minutes as shown in Table 1 (column 4) under post-prandial glucose test,

characteristic dose-dependent durations of the LT's differences with CBG for glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} under any OGTT with different doses of 5 g, 20 g and 75 g glucose,

characteristic single-, bi- and three-phase LT's differences for 1030-1041 cm^{-1} at 0 and 10 minutes, for 1080 cm^{-1} at 10 minutes, for 1118 cm^{-1} at 0, 10 and 25 minutes, for 1153 cm^{-1} at 15 and 25 minutes under OGTT (5 g),

characteristic single- and bi-phase LT's and their calculated differences with CBG for 1030-1041 cm^{-1} at 0 minutes, for 1080 cm^{-1} at 15 minutes, for 1118 cm^{-1} at 5 minutes, for 1153 cm^{-1} at 15 and 40 minutes under OGTT (20 g),

characteristic single-phase LT's and their calculated differences with CBG for 1030-1041 cm^{-1} at 0 minutes, for 1080 cm^{-1} at 0 minutes, for 1118 cm^{-1} at 0 minutes, for 1153 cm^{-1} at 30 minutes under OGTT (75 g),

the time duration of the LT's differences of within 0-30 minutes with characteristic predominant single-phase detection at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, as compared under OGTT with 75 g for a prediabetic subject with the LT's differences of within 0-55 minutes with characteristic multi-phase cascade detection at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} on HATR-FTIR spectrometer as shown in Table 7 (column 3), or as compared with the LT differences with the time duration of within 5-50 minutes with characteristic single- and/or bi-phase detection at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, to be specific for a diabetic subject.

2. A method of monitoring the spectral pattern of individual metabolic response by a continuous monitoring of GV and/or by measuring the LT and the LT difference for each glucose-specific peak at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g, occasionally and/or on consecutive days, to provide information needed for diagnosing, screening or predicting disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being on HATR-FTIR

spectrometer, or for screening and follow-up a development of a diabetes in a healthy subject except for a human being, or for screening and follow-up a development of a diabetes in a subject with a prediabetes except for a human being, or for predicting the subject's risk of hyperglycemia, or for staging Type 2 diabetes in a patient except for a human being, or for managing a subject with or without hyperglycemia, or for assessing the quality of metabolic control in a subject except for a human being, or for determining the most effective therapy in a subject with a Type 2 diabetes except for a human being, or for determining the most effective dosage of drug in a subject with a Type 2 diabetes except for a human being, the method comprising the steps according to Claim 1, and

(xi) monitoring the change of the spectral pattern of individual metabolic response by a continuous monitoring of GV in correlation with characteristic spectral parameters for glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} identified in step (v) and/or the change of the spectral pattern of individual metabolic response by measuring the LTs and the LTs differences with CBG in correlation with characteristic spectral parameters identified in step (x) for stratifying the patient as having, or being at the risk of developing, a diabetes, to a screening and follow-up regimen for preventing a diabetes in said subject except for a human being or for preventing a development towards a diabetes in said subject except for a human being,

wherein the change of the spectral pattern of individual metabolic response by a continuous monitoring of GV in correlation with characteristic spectral parameters for glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} identified in step (v) for a healthy subject or for a prediabetic subject to the spectral pattern of individual metabolic response by a continuous monitoring of GV in correlation with characteristic spectral parameters for glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} identified in step (v) for a diabetic subject except for a

human being, indicates a diabetes in said subject except for a human being, and/or

the change of the spectral pattern of individual metabolic response by measuring the LTs and the LTs differences with CBG in correlation with characteristic spectral parameters identified in step (x) for a healthy subject or for a prediabetic subject to the change of the spectral pattern of individual metabolic response by measuring the LTs and the LTs differences with CBG in correlation with characteristic spectral parameters identified in step (x) for a diabetic subject except for a human being, indicates a diabetes in said subject except for a human being,

or

(xii) monitoring the change of the spectral pattern of individual metabolic response by a continuous monitoring of GV in correlation with characteristic spectral parameters for glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} identified in step (v) and/or monitoring the change of the spectral pattern of individual metabolic response by measuring the LTs and the LTs differences with CBG in correlation with characteristic spectral parameters identified in step (x) for stratifying the subject as having, or being at the risk of developing, a diabetes, to a therapeutic regimen for treating or preventing a diabetes in said subject except for a human being.

3. Use of HATR-FTIR spectrometer for recognizing the spectral pattern of individual metabolic response by a continuous monitoring of glycemic variability (GV) and its spectral characteristics on a subject except for a human being under post-prandial glucose test and/or Oral Glucose Tolerance Test (OGTT) with different doses of 5 g, 20 g and/or 75 g (low, medium, high) and for recognizing the spectral pattern of individual metabolic response by measuring the LT and the LT difference with CBG for each assigned glucose-specific peak under post-prandial glucose test

and/or OGTT at the different doses of 5 g, 20 g and/or 75 g (low, medium, high) in order to diagnose disorders of glucose metabolism in a subject except for a human being, or to screen and follow-up disorders of glucose metabolism in a subject except for a human being, or to predict the subject's risk of hyperglycemia, or to stage Type 2 diabetes in a subject except for a human being, or to manage a subject with or without hyperglycemia except for a human being, or to assess the quality of metabolic control in a subject except for a human being, or to manage disorders of glucose metabolism in a subject except for a human being, or to treat disorders of glucose metabolism in a subject except for a human being, by spectral patterned data analysis for evaluating individual metabolic response and for generating predictive clinical metrics by a continuous monitoring of GV in correlation with characteristic spectral parameters for glucose-specific peaks at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} identified in step (v) on HATR-FTIR spectrometer and/or the change of the spectral pattern of individual metabolic response by measuring the LTs and the LTs differences with CBG in correlation with characteristic spectral parameters identified in step (x) on HATR-FTIR spectrometer, comprising the steps according to any of Claims 1-3.

4. The method of any of Claims 1-2, or the device of Claim 3, wherein said carbohydrate metabolism disorders are selected from the group of prediabetes and Type 2 diabetes, are also applicable to other disorders of carbohydrate metabolism.

5. A glucose molecule with characteristic spectral parameters at consistent and significant absorption wave number at 1030 cm^{-1} or 1041 cm^{-1}, characterized by spectral bounded bands of glucose in the mid-IR spectra corresponding to identity and structures to glucose molecules in correlation with characteristic measurements of the peak position and/or its shift, the peak levels on HATR-FTIR spectrometer in the interstitial fluid of the epidermal skin tissue of a healthy, prediabetic or diabetic subject under

post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g, when used for evaluating individual metabolic response and for generating predictive clinical metrics needed for diagnosing disorders of glucose metabolism, such as prediabetes and diabetes, or for screening and follow-up of disorders of glucose metabolism, such as prediabetes and diabetes, which is one selected from:

(i) a glucose molecule with

characteristic predominant mean peak position near 1030 cm^{-1} within 1030-1041 cm^{-1} according to Figure 8 c-e and Figure 11 a,

characteristic the highest glucose peak levels within 1030-1041 cm^{-1} over the other glucose peaks levels at 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} according to Figure 8 c-e,

characteristic indifferentiated to low, medium and high glucose dose peak levels under OGTT with 5 g, 20 g and/or 75 g according to Figure 5 a,

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 15 and 30 minutes under OGTT (5 g) with reference to Table 2 (column 3, row 2),

characteristic single-phase LTs and the LTs differences with CBG with the time intervals of 10 minutes under OGTT (20 g) with reference to Table 2 (column 4, row 2) in Example 2,

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 5 and 30 minutes under OGTT (75 g) with reference to Table 2 (column 5, row 2),

to be specific for a healthy subject; or

(ii) a glucose molecule with

characteristic predominant mean peak position near 1037-1041 cm^{-1} within 1030 - 1041 cm^{-1} according to Figure 8 f and Figure 11 a,

characteristic the highest glucose peak levels within 1030 - 1041 cm^{-1} similar to the peak levels at 1118 cm^{-1} according to Figure 8 f,

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characteristic dose-differentiated peak levels to high dose of glucose at 75 g under OGTT (75 g) according to Figure 8 f and Figure 11 a,

characteristic multi-phase LTs and the LTs differences with CBG with the time intervals of 5, 20, 30 and 45 minutes under OGTT (75 g) with reference to Table 7 (column 3, row 2),

to be specific for a prediabetic subject; or

(iii) a glucose molecule with

characteristic predominant mean peak position near 1039-1041 cm^{-1} within 1030 - 1041 cm^{-1} according to Figure 11 a,

characteristic differentiated to low, medium and high glucose dose peak levels under OGTT with 5 g, 20 g and/or 75 g according to Figure 6 a,

characteristic single-phase LTs and the LTs differences with CBG with the time intervals of 0 minutes under post-prandial glucose test according to Table 1 (column 2, rows 1-4), Figures 2 a, 3 a and 4 a,

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 0 and 10 minutes under OGTT (5 g) with reference to Table 3 (column 3, row 2),

characteristic single-phase LTs and the LTs differences with CBG with the time intervals of 0 minutes under OGTT (20 g) with reference to Table 3 (column 4, row 2),

characteristic single-phase LTs and the LTs differences with CBG with the time intervals of 0 minutes under OGTT (75 g) with reference to Table 3 (column 5, row 2),

to be specific for a diabetic subject.

6. A glucose molecule with characteristic spectral parameters at consistent and significant absorption wave number at 1080 cm^{-1}, characterized by spectral band of glucose in the mid-IR spectra corresponding to identity and structures to glucose molecules in correlation with characteristic measurements of the peak position and/or its shift, the

peak levels on HATR-FTIR spectrometer in the interstitial fluid of the epidermal skin tissue of a healthy, prediabetic or diabetic subject under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g, when used for evaluating individual metabolic response and for generating predictive clinical metrics needed for diagnosing disorders of glucose metabolism, such as prediabetes and diabetes, or for screening and follow-up of disorders of glucose metabolism, such as prediabetes and diabetes, which is one selected from:

(i) a glucose molecule with

characteristic indifferentiated peak levels to low, medium and high glucose doses under OGTT with 5 g, 20 g and/or 75 g according to Figure 5 b,

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 15 and 30 minutes under OGTT (5 g) with reference to Table 2 (column 3, row 3),

characteristic three-phase LTs and the LTs differences with CBG with the time intervals of 0, 10 and 20 minutes under OGTT (20 g) with reference to Table 2 (column 4, row 3),

characteristic single-phase LTs and the LTs differences with CBG with the time intervals of 5 minutes under OGTT (75 g) with reference to Table 2 (column 5, row 3),

to be specific for a healthy subject; or

(ii) a glucose molecule with

characteristic differentiated peak levels to high glucose dose under OGTT with 75 g according to Figure 11 b,

characteristic three-phase LTs and the LTs differences with CBG with the time intervals of 5, 20 and 45 minutes under OGTT (75 g) with reference to Table 7 (column 3, row 3),

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to be specific for a prediabetic subject; or

(iii) a glucose molecule with

characteristic dose-differentiated peak levels to low, medium and high glucose dose under OGTT with 5 g, 20 g and/or 75 g according to Figure 6 b,

characteristic single-phase LTs and the LTs differences with CBG with the time interval of 10 minutes under OGTT (5 g) with reference to Table 3 (column 3, row 3),

characteristic single-phase LTs and the LTs differences with CBG with the time interval of 15 minutes under OGTT (20 g) with reference to Table 3 (column 4, row 3),

characteristic single-phase LTs and the LTs differences with CBG with the time interval of 0 minutes under OGTT (75 g) with reference to Table 3 (column 5, row 3) and to Table 7 (column 4, row 3),

to be specific for a diabetic subject.

7. A glucose molecule with characteristic spectral parameters at consistent and significant absorption wave number at 1118 cm^{-1}, characterized by spectral band of glucose in the mid-IR spectra corresponding to identity and structures to glucose molecules in correlation with characteristic measurements of the peak position and/or its shift, the peak levels on HATR-FTIR spectrometer in the interstitial fluid of the epidermal skin tissue of a healthy, prediabetic or diabetic subject under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g, when used for evaluating individual metabolic response and for generating predictive clinical metrics needed for diagnosing disorders of glucose metabolism, such as prediabetes and diabetes on a subject except for a human being, or for screening and follow-up of disorders of glucose

metabolism, such as prediabetes and diabetes on a subject except for a human being, which is one selected from:

(i) a glucose molecule with

characteristic predominant left-shifted mean peak position within 1114-1118 cm^{-1} according to Figure 5 c, wherein mean peak position near 1118 cm^{-1} is characteristic under OGTT with 5 g, mean peak position near 1114-1118 cm^{-1} is characteristic under OGTT with 20 g, mean peak position near 1116-1118 cm^{-1} is characteristic under OGTT with 75 g,

characteristic indifferentiated peak levels to low, medium and high glucose dose under OGTT with 5 g, 20 g and/or 75 g according to Figure 5 c,

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 10 and 25 minutes under OGTT (5 g) with reference to Table 2 (column 3, row 4),

characteristic single-phase LTs and the LTs differences with CBG with the time intervals of 10 minutes under OGTT (20 g) with reference to Table 2 (column 4, row 4),

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 5 and 25 minutes under OGTT (75 g) with reference to Table 2 (column 5, row 4),

to be specific for a healthy subject; or

(ii) a glucose molecule with

characteristic predominant right-shifted mean peak position within 1120-1122 cm^{-1} according to Figure 8 f,

characteristic the highest glucose peak levels similar to glucose peak levels at 1030 - 1041 cm^{-1} over the other 2 glucose peak levels at 1080 cm^{-1} and 1153 cm^{-1} according to Figure 8 f,

characteristic dose-differentiated peak levels to high dose of glucose at 75 g under OGTT (75 g) according to Figure 8 f and Figure 11 c,

characteristic cascading multi-phase LTs and the LTs differences with CBG with the time intervals of 5, 20, 30 and 40 minutes under OGTT (75 g) with reference to Table 7 (column 3, row 4),

to be specific for a prediabetic subject; or

(iii) a glucose molecule with

characteristic dominant right-shifted mean peak position within 1120-1122 cm^{-1} according to Figures 6 c, 8 a, 8 c and 11 c,

characteristic the highest glucose peak levels within 1120-1122 cm^{-1} over the other glucose peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1153 cm^{-1} according to Figure 8 b and Figure 11 c,

characteristic dose-differentiated peak levels to low, medium and high doses of glucose at 5 g, 20 g and 75 g under OGTT (5 g, 20 g, 75 g) according to Figure 6 c and Figure 7 b,

characteristic three-phase LTs and the LTs differences with CBG with the time intervals of 0, 10 and 25 minutes under OGTT (5 g) with reference to Table 3 (column 3, row 4),

characteristic single-phase LTs and the LTs differences with CBG with the time intervals of 5 minutes under OGTT (20 g) with reference to Table 3 (column 4, row 4),

characteristic single-phase LTs and the LTs differences with CBG with the time intervals of 0 minutes under OGTT (75 g) with reference to Table 3 (column 5, row 4),

to be specific for a diabetic subject.

8. A glucose molecule with characteristic spectral parameters at consistent and significant absorption wave number at 1153 cm^{-1}, characterized by spectral band of glucose in the mid-IR spectra corresponding to identity and structures to glucose molecules in correlation with characteristic measurements of the peak position and/or its shift, the

peak levels on HATR-FTIR spectrometer in the interstitial fluid of the epidermal skin tissue of a healthy, prediabetic or diabetic subject under post-prandial glucose test and/or OGTT at the different doses of 5 g, 20 g and/or 75 g, when used for evaluating individual metabolic response and for generating predictive clinical metrics needed for diagnosing disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, or for screening and follow-up of disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, which is one selected from:

(i) a glucose molecule with

characteristic predominant left-shifted mean peak position within 1149-1153 cm^{-1} according to Figure 8 e,

characteristic the lowest glucose peak levels near 1153 cm^{-1} below the other glucose peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 e,

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 35 and 50 minutes under OGTT (5 g) with reference to Table 2 (column 3, row 5),

characteristic single-phase LTs and the LTs differences with CBG with the time intervals of 10 and 15 minutes under OGTT (20 g) with reference to Table 2 (column 4, row 5),

characteristic single-phase LTs and the LTs differences with CBG with the time intervals of 10 minutes under OGTT (75 g) with reference to Table 3 (column 5, row 5),
to be specific for a healthy subject; or

(ii) a glucose molecule with

characteristic the lowest glucose peak levels near 1153 cm^{-1} below the other glucose peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 f and Figure 11 d,

characteristic cascading multi-phase LTs and the LTs differences with CBG with the time intervals of 0, 15, 25 and 55 minutes under OGTT (75 g) with reference to Table 7 (column 3, row 5),

to be specific for a prediabetic subject; or

(iii) a glucose molecule with

characteristic predominant right-shifted mean peak position within 1153-1157 cm^{-1} according to Figure 8 b,

characteristic the lowest glucose peak levels near 1153 cm^{-1} below the other glucose peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 f and Figure 11 d,

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 15 and 25 minutes under OGTT (5 g) with reference to Table 3 (column 3, row 5),

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 25 and 40 minutes under OGTT (20 g) with reference to Table 3 (column 4, row 5),

characteristic bi-phase LTs and the LTs differences with CBG with the time intervals of 30 minutes under OGTT (75 g) with reference to Table 3 (column 5, row 5),

to be specific for a diabetic subject.

9. A combination group of glucose molecules with characteristic spectral parameters at consistent and significant absorption wave number at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, characterized by spectral bands of glucose in the mid-IR spectra corresponding to identity and structures to glucose molecules in correlation with characteristic measurements of the peaks position and/or their shift, the peaks levels on HATR-FTIR spectrometer in the interstitial fluid of the epidermal skin tissue of a healthy, prediabetic or diabetic subject under post-prandial glucose test

and/or OGTT at the different doses of 5 g, 20 g and/or 75 g, when used for evaluating individual metabolic response and for generating predictive clinical metrics needed for diagnosing disorders of glucose metabolism, such as prediabetes and diabetes on a subject except for a human being, or for screening and follow-up of disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, which is one selected from:

(i) a combination group of glucose molecules with

characteristic the highest peak levels at 1030-1041 cm^{-1} over the other 3 glucose-specific peak levels according to Figure 8 c and 8 d,

characteristic the lowest glucose peak levels near 1153 cm^{-1} below the other glucose peaks levels at 1030-1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} according to Figure 8 e,

characteristic indifferentiated to dose-response peak levels at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and/or 1153 cm^{-1},

characteristic bi-phase LT's differences for 1030-1041 cm^{-1} at 15 and 30 minutes, for 1080 cm^{-1} at 15 and 30 minutes, for 1118 cm^{-1} at 10 and 25 minutes, and for 1153 cm^{-1} at 35 and 50 minutes under OGTT (5 g) with reference to Table 2 (column 3),

characteristic single-, bi- and three-phase LT's differences for 1030-1041 cm^{-1} at 10 minutes, for 1080 cm^{-1} at 0, 10 and 20 minutes, for 1118 cm^{-1} at 10 minutes, for 1153 cm^{-1} at 10 and 15 minutes under OGTT (20 g) with reference to Table 2 (column 4),

characteristic single- and bi-phase LT's differences for 1030-1041 cm^{-1} at 5 and 30 minutes, for 1080 cm^{-1} at 5 minutes, for 1118 cm^{-1} at 5 and 25 minutes, and for 1153 cm^{-1} at 10 minutes under OGTT (75 g) with reference to Table 2 (column 5),

to be specific for a healthy subject; or

(ii) a combination group of glucose molecules with

characteristic multi-phasic LT's differences for 1030-1041 cm⁻¹ at 5, 20, 30 and 45 minutes, for 1080 cm⁻¹ at 5, 20 and 45 minutes, for 1118 cm⁻¹ at 5, 20, 30 and 40 minutes, and for 1153 cm⁻¹ at 0, 15, 25 and 55 minutes under OGTT (75 g) with reference to Table 7 (column 3),

to be specific for a prediabetic subject; or

(iii) a combination group of glucose molecules with

characteristic comparative dose-dependent GV dynamics of glucose peak levels at 1030 - 1041 cm⁻¹, 1080 cm⁻¹ and 1118 cm⁻¹ according to Figure 6 a-c during OGTT with different doses of glucose, wherein said glucose peaks levels are dose-dependent and well-differentiated between intaken doses of glucose from starting to the ending point of the test;

characteristic predominant high glucose peak levels at 1118 cm⁻¹ over the other glucose peaks levels according to Figure 8 a-b,

characteristic predominant glucose peak position at 1041 cm⁻¹ within 1030 - 1041 cm⁻¹ according to Figure 6 a, Figure 8 a-b and Figure 11 a,

characteristic dominant right-shifted mean positions of the peak at 1118 cm⁻¹ according to Figure 6 c, Figure 7 a-b, Figure 8 a-b and Figure 11 c,

characteristic differences in the levels of glucose values and/or wavenumber shifts at 1030 - 1041 cm⁻¹, 1080 cm⁻¹, 1118 cm⁻¹, and/or 1153 cm⁻¹ obtained at the different glucose doses as compared with characteristic differences for healthy and diabetic subjects as shown in Figure 7 a-c, Figure 9 a-d and Figure 11 a-d,

characteristic single-, bi- and three-phase LTs differences for 1030-1041 cm^{-1} at 0 and 10 minutes, for 1080 cm^{-1} at 10 minutes, for 1118 cm^{-1} at 0, 10 and 25 minutes, for 1153 cm^{-1} at 15 and 25 minutes under OGTT (5 g) with reference to Table 3 (column 3),

characteristic single- and bi-phase LTs differences within 1030-1041 cm^{-1} at 0 minutes, for 1080 cm^{-1} at 15 minutes, for 1118 cm^{-1} at 5 minutes, and for 1153 cm^{-1} at 15 and 40 minutes under OGTT (20 g) with reference to Table 5 (column 3),

characteristic single-phase LT's differences for 1030-1041 cm^{-1} at 0 minutes, for 1080 cm^{-1} at 0 minutes, for 1118 cm^{-1} at 0 minutes, for 1153 cm^{-1} at 30 minutes under OGTT (75 g) with reference to Table 7 (column 4),

to be specific for a diabetic subject.

10. A glucose molecule selected with characteristic spectral parameter at consistent and significant absorption wave number at 1030 cm^{-1} or 1041 cm^{-1} on HATR-FTIR spectrometer for diagnosing disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, or for screening and follow-up disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, or for treating disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, selected from one of the glucose molecules, comprising its spectral characteristics according to Claim 7.

11. A glucose molecule with characteristic spectral parameter at consistent and significant absorption wave number at 1080 cm^{-1} on HATR-FTIR spectrometer for diagnosing disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, or for screening and follow-up disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, or for

treating disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, selected from one of the glucose molecules, comprising its spectral characteristics according to Claim 8.

12. A glucose molecule with characteristic spectral parameter at consistent and significant absorption wave number at 1118 cm^{-1} on HATR-FTIR spectrometer for diagnosing disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, or for screening and follow-up disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, or for treating disorders of glucose metabolism, such as prediabetes and diabetes, on a subject except for a human being, selected from one of the glucose molecules, comprising its spectral characteristics according to Claim 9.

13. A combination group of glucose molecules with characteristic spectral parameters at consistent and significant absorption wave number at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1}, 1153 cm^{-1} on HATR-FTIR spectrometer for diagnosing disorders of glucose metabolism, such as prediabetes and diabetes on a subject except for a human being, or for screening and follow-up disorders of glucose metabolism, such as prediabetes and diabetes on a subject except for a human being, or for treating disorders of glucose metabolism, such as prediabetes and diabetes on a subject except for a human being, selected from one of the glucose molecules, comprising its spectral characteristics, selected from one of the combination groups, comprising its spectral characteristics according to Claim 11.

200192429

FORM 2
THE PATENT ACT 1970
(39 of 1970)
&
The Patents Rules, 2003
PROVISIONAL/COMPLETE SPECIFICATION
(See section 10 and rule13)

1. TITLE OF THE INVENTION METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE AND FOR GENERATING PREDICTIVE CLINICAL METRICS:

2. APPLICANT (S)
(a) NAME: NATALJA EIKJE
(b) NATIONALITY: ESTONIA / NORWAY
(c) ADDRESS: 412-B, 4TH FLOOR, UNITECH ARCADIA Building, SECTOR 49, SOUTH CITY-2, GURGAON 122018, INDIA

3. PREAMBLE TO THE DESCRIPTION

~~PROVISIONAL~~	COMPLETE
The following specification describes the invention.	The following specification particularly describes the invention and the manner in which it is to be performed.

4. DESCRIPTION (Description shall start from next page.)
ON PAGES 1 to 15 (NO EXCESS PAGES) - SPECIFICATION (WITH INCORPORATED AMENDED TITLE);
ON PAGES 1 to 20 (DRAWINGS) (EXCESS 5 pages (180 Rps x 5) 900 Rps

5. CLAIMS (not applicable for provisional specification. Claims should start with the preamble — **"I/we claim"** on separate page) ON PAGES 1 to 25,
AMENDED Claims 1 to 13 (excess 3 claims, paid 350 Rps x 3 (1050 Rps))

6. DATE AND SIGNATURE (to be given at the end of last page of specification)

7. ABSTRACT OF THE INVENTION (to be given along with complete specification on separate page)
ON ~~SEPARATE~~ PAGE 16 (WITH INCORPORATED AMENDED TITLE)

Note: -
 *Repeat boxes in case of more than one entry.
 *To be signed by the applicant(s) or by authorized registered patent agent.
 *Name of the applicant should be given in full, family name in the beginning .
 *Complete address of the applicant should be given stating the postal index no./code, state and country.
 *Strike out the column which is/are not applicable

1796 / MUMNP / 2014

Fig. 1

Fig. 2A

Fig. 2B

IPO MUMBAI 16-07-2018 17:57

Fig. 2C

Fig. 2D

Fig. 3A

Fig. 3B

Fig. 3C

Fig. 3D

Fig. 4A

Fig. 4B

Fig.4C

Fig. 4D

HEALTHY

Fig. 5A

HEALTHY

Fig. 5B

Fig. 5C

Fig. 6A

Fig. 6B

Fig. 6C

Fig. 7A

Fig. 7B

Fig. 7C

Fig. 8A

Fig. 8B

Fig. 8C

Fig. 8D

Fig. 8E

Fig. 8F

Fig. 9A

Fig. 9B

Fig. 9C

Fig. 10A

SUBJECT 3, 1030-1041 cm⁻¹
−□− DAY 1
−○− DAY 2

Fig. 10B

SUBJECT 3, 1080 cm⁻¹
−□− DAY 1
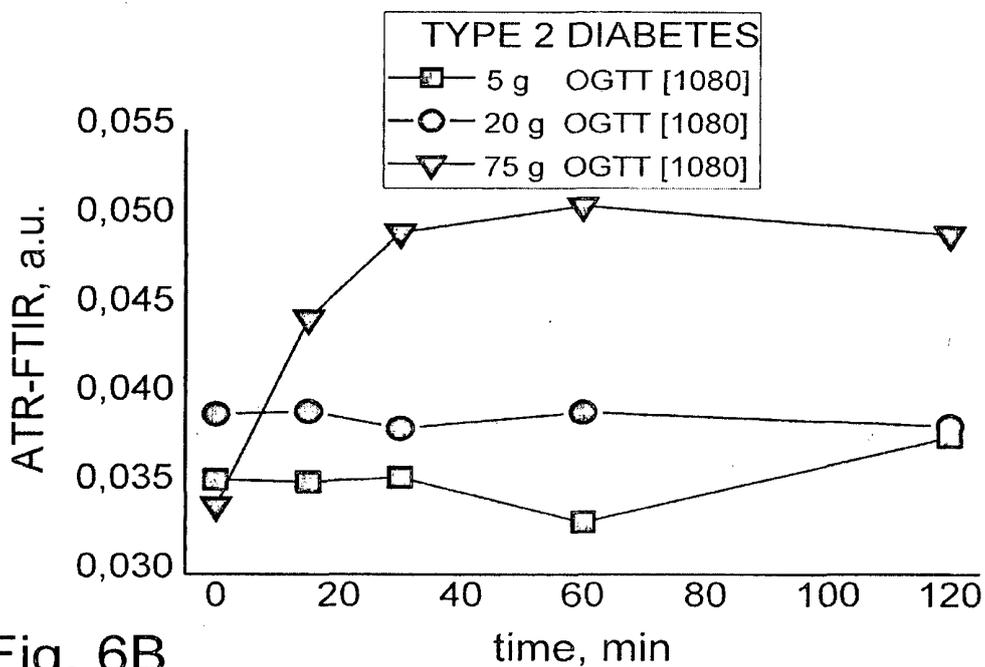−○− DAY 2
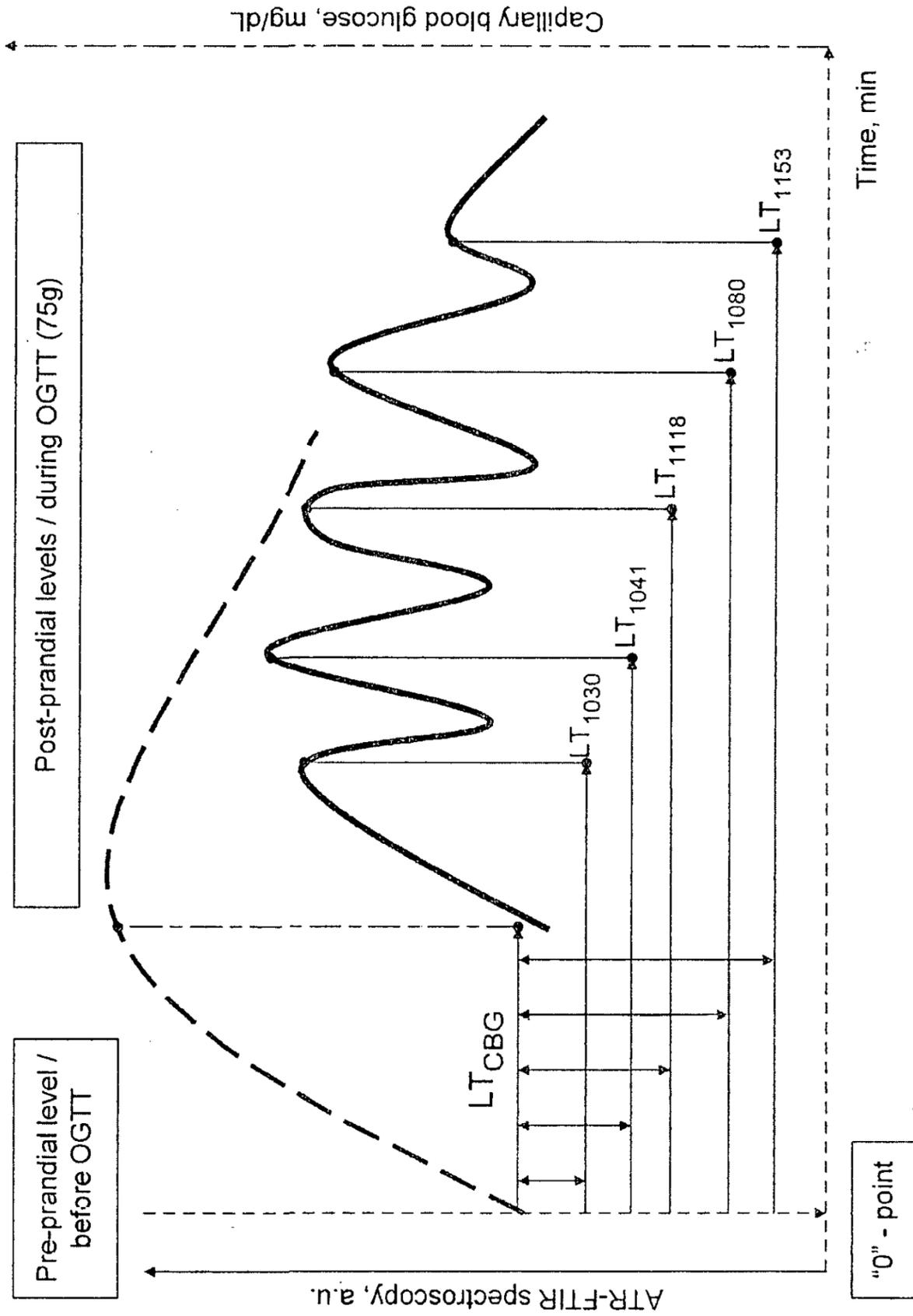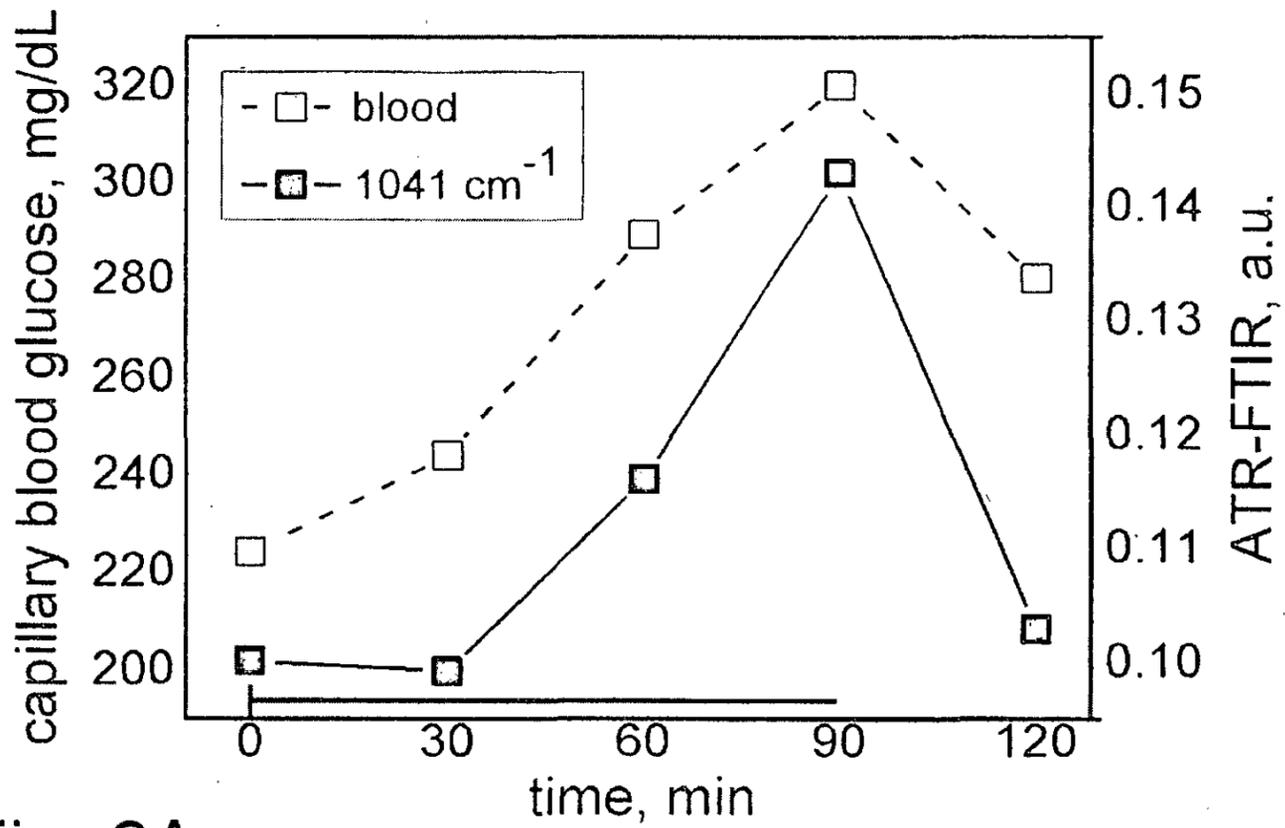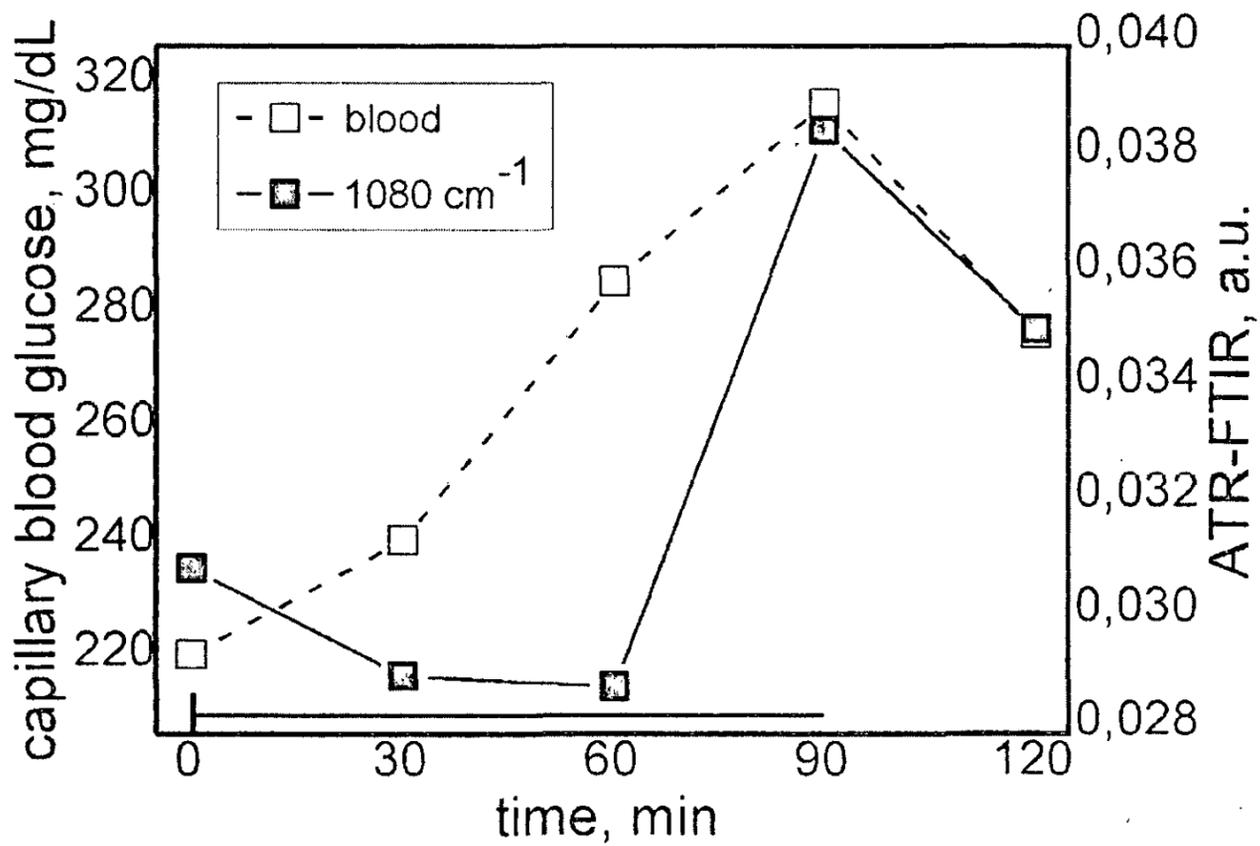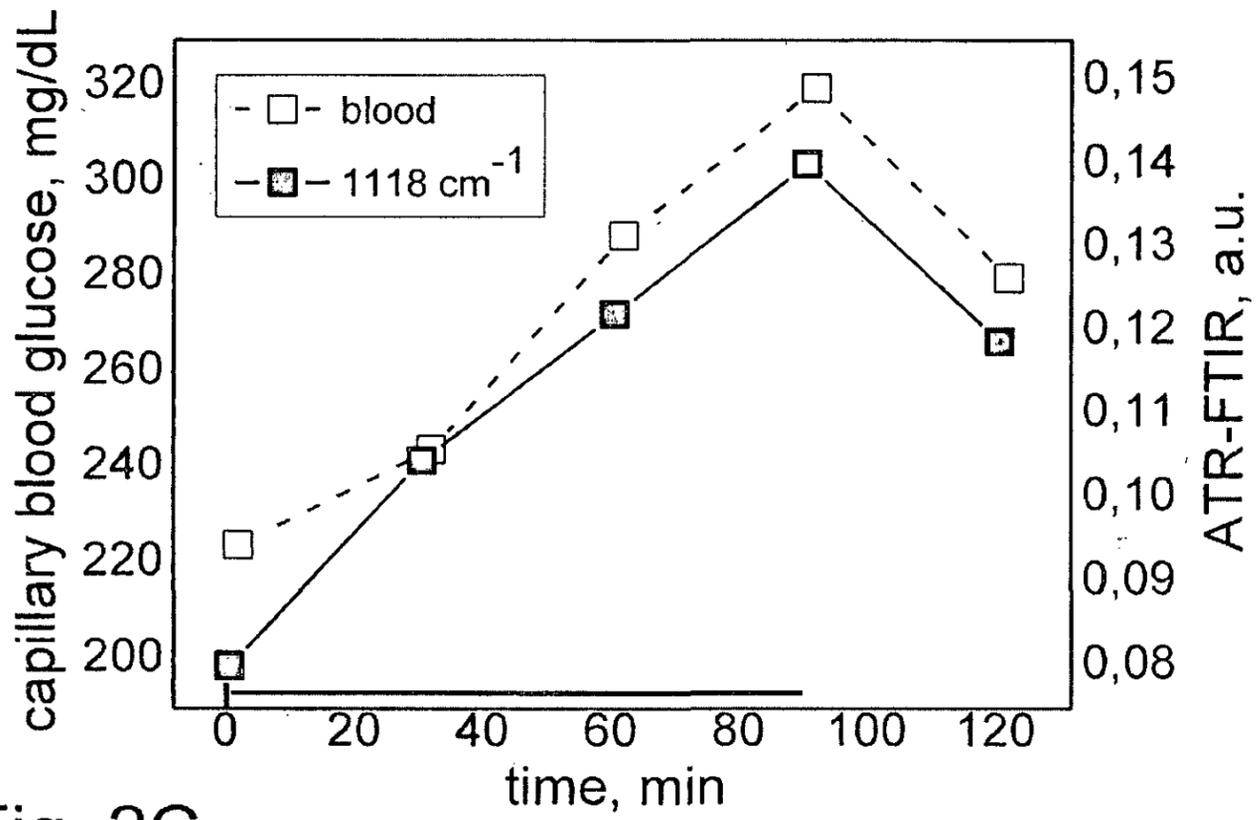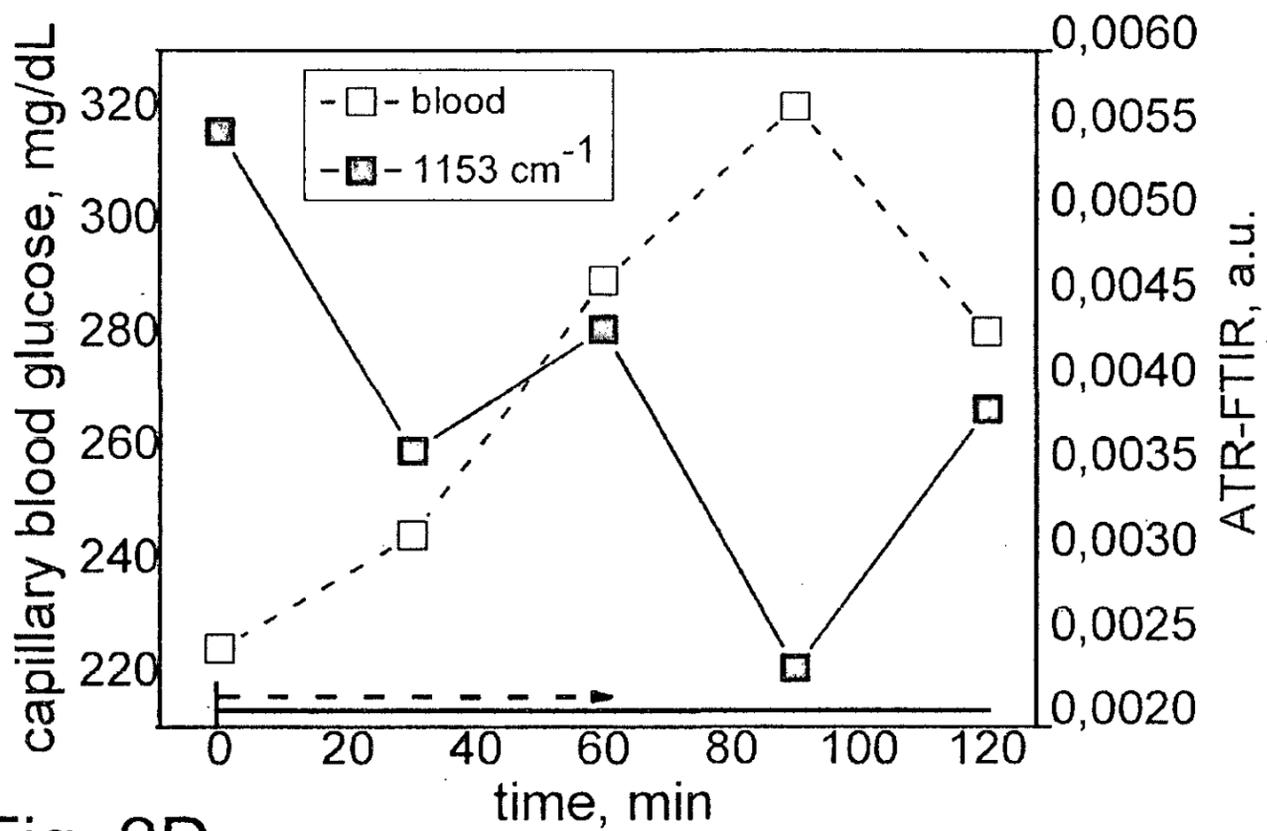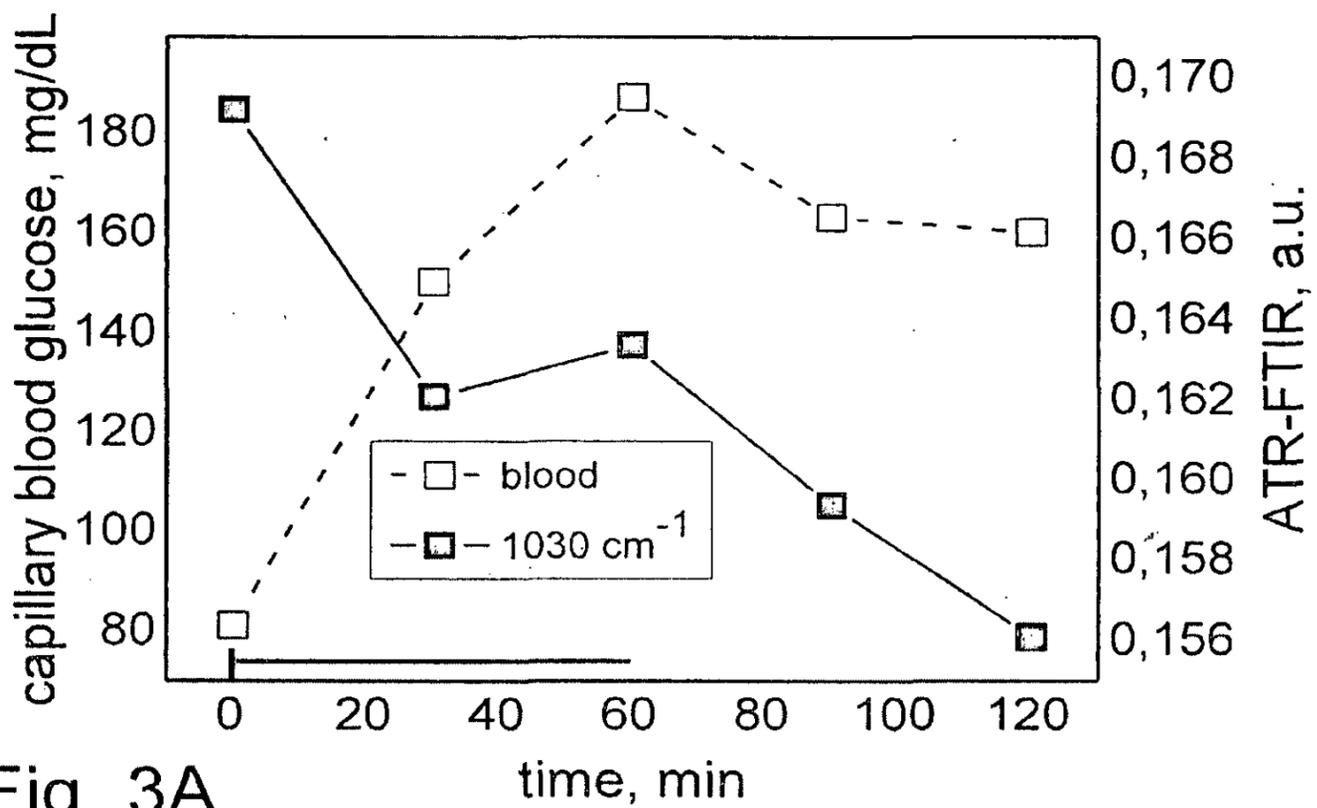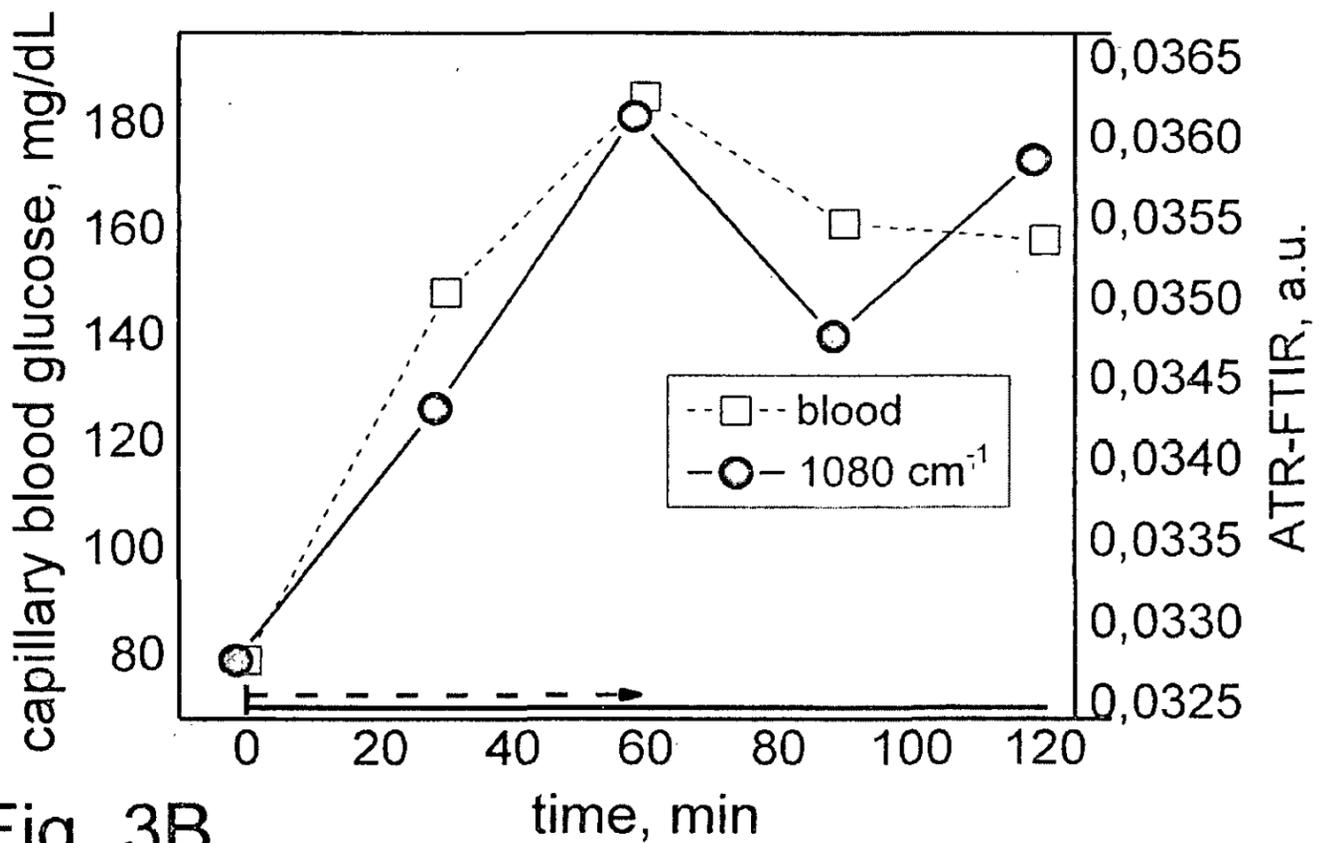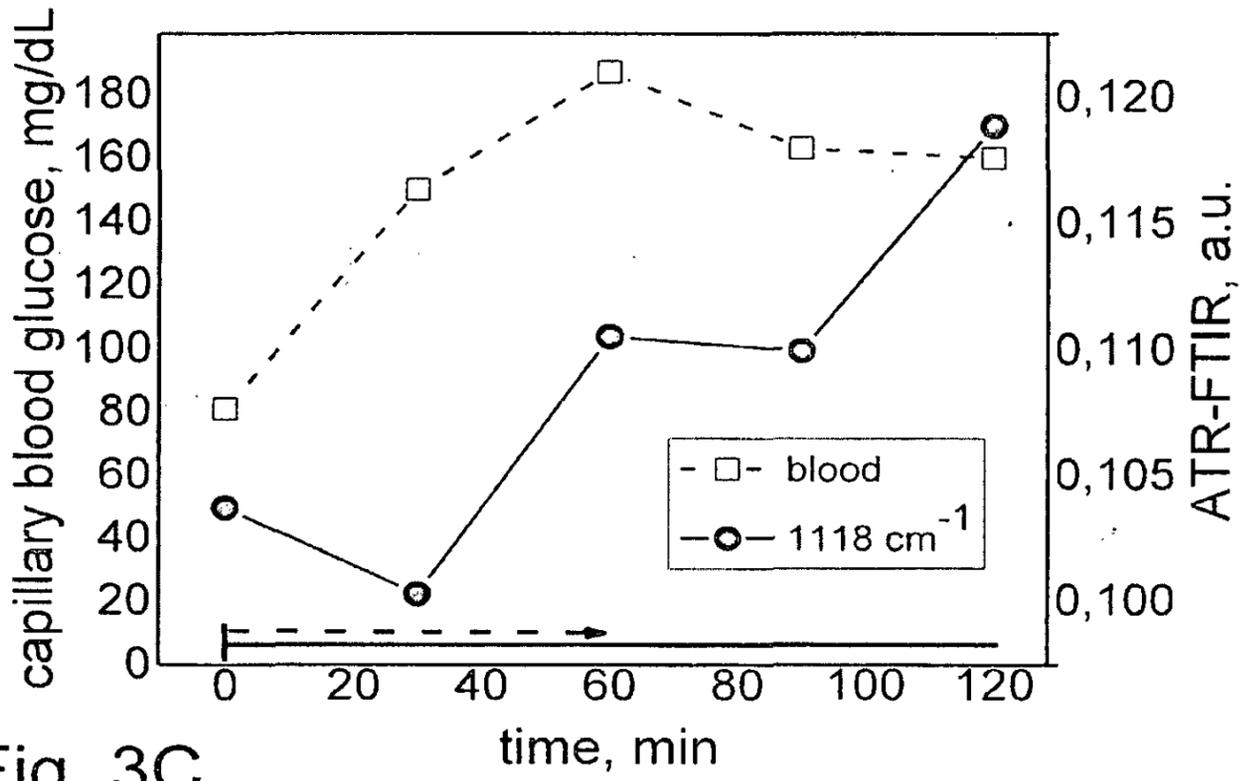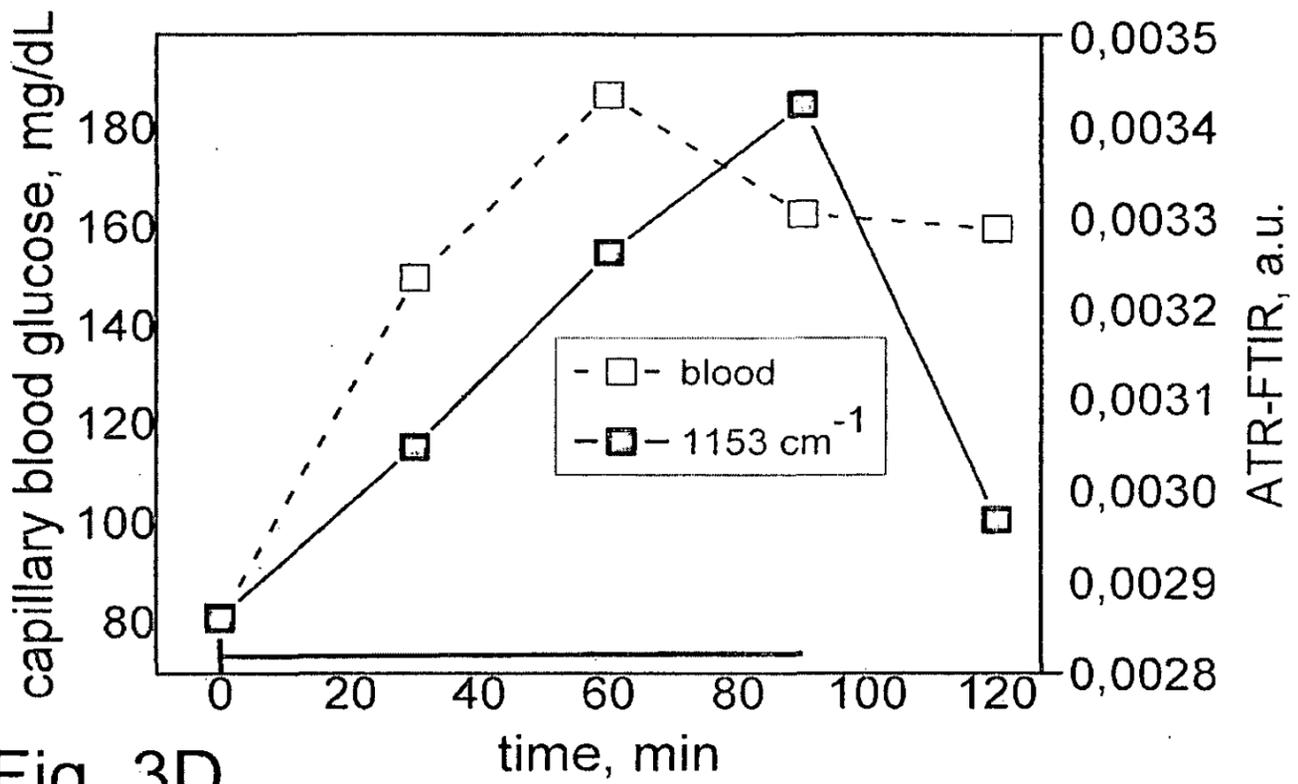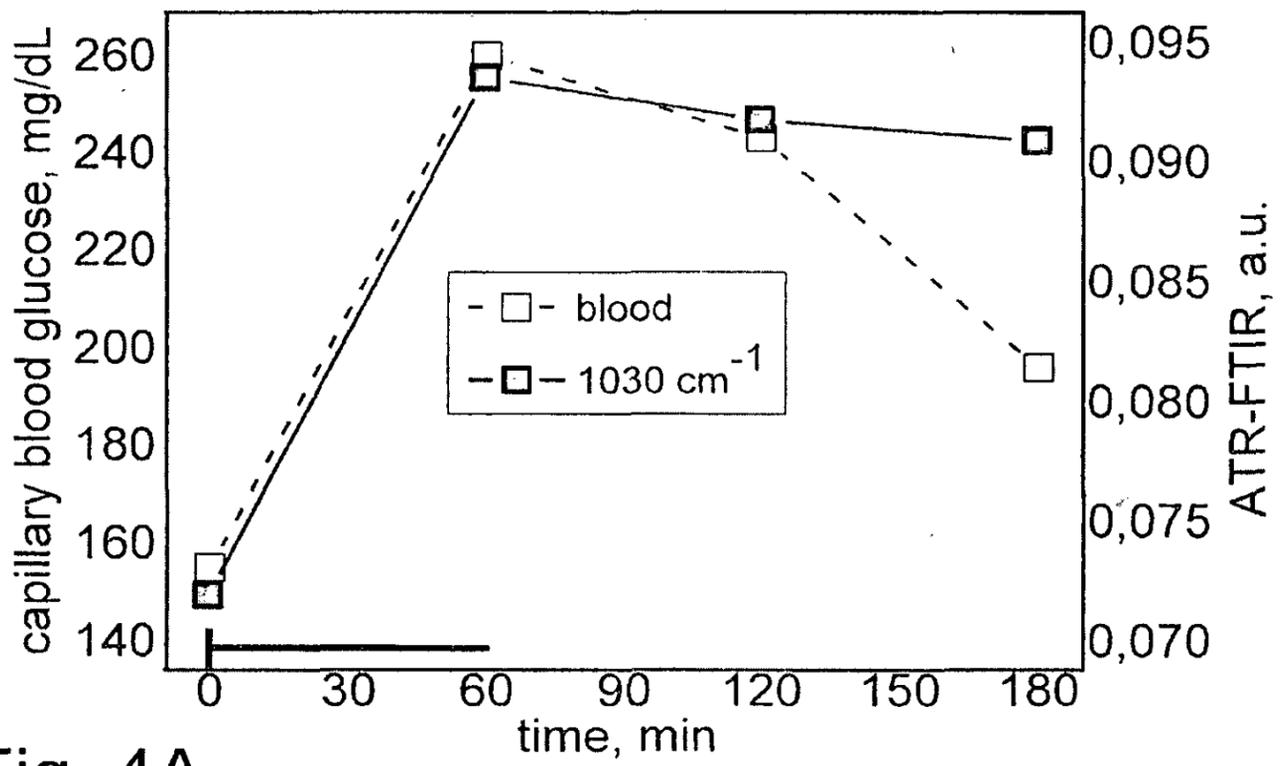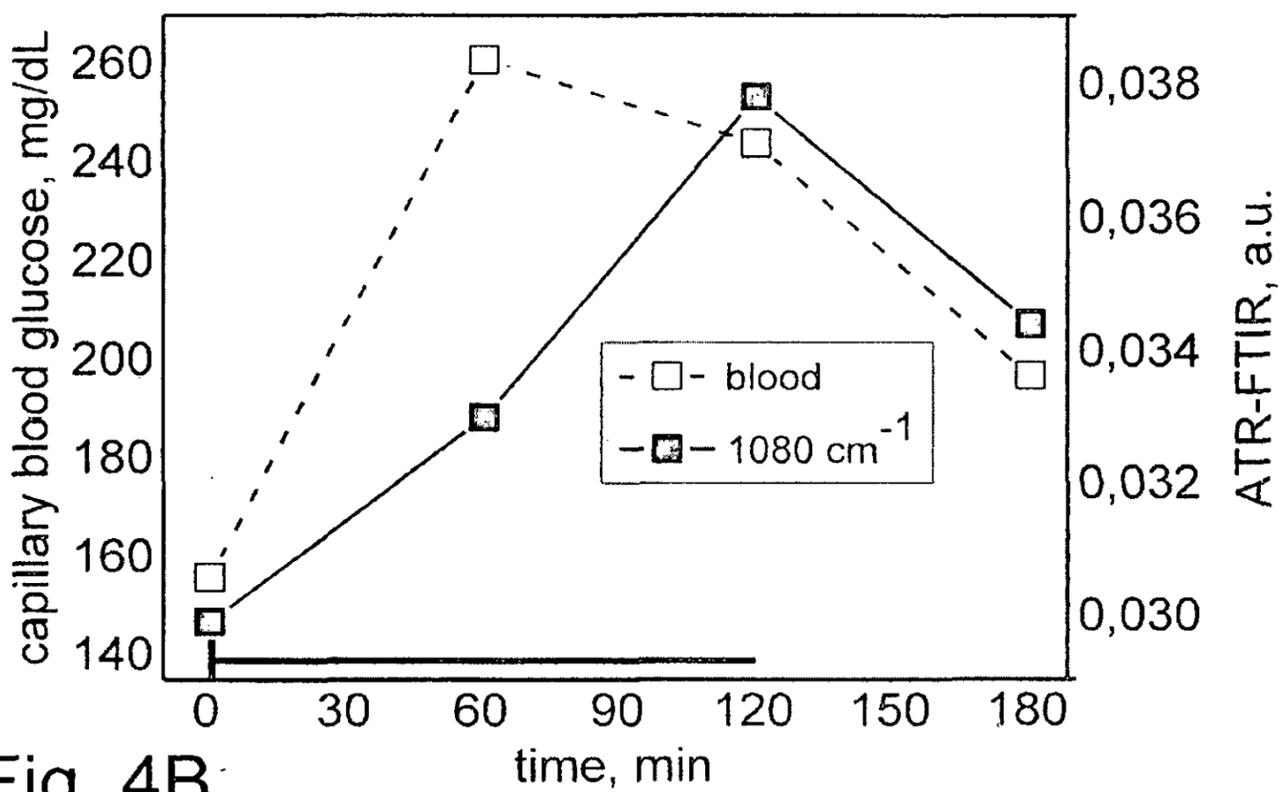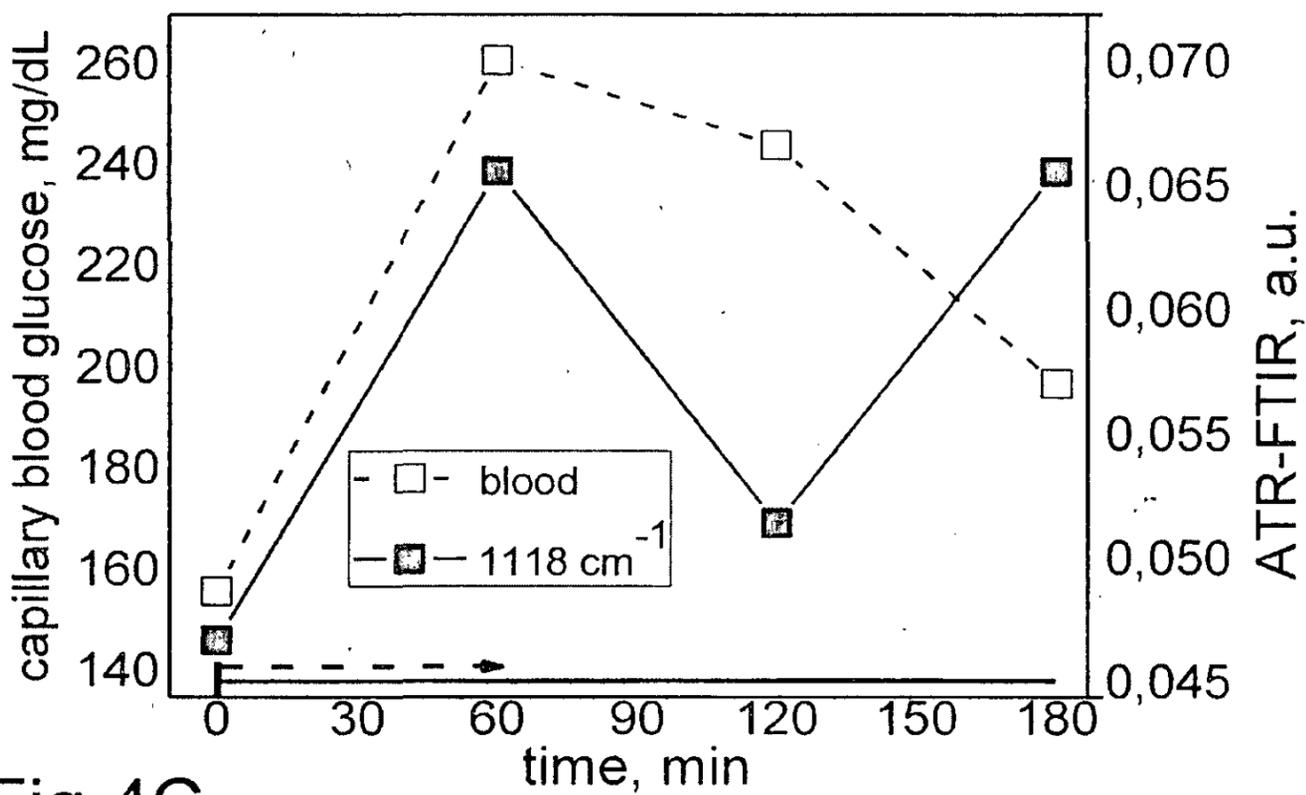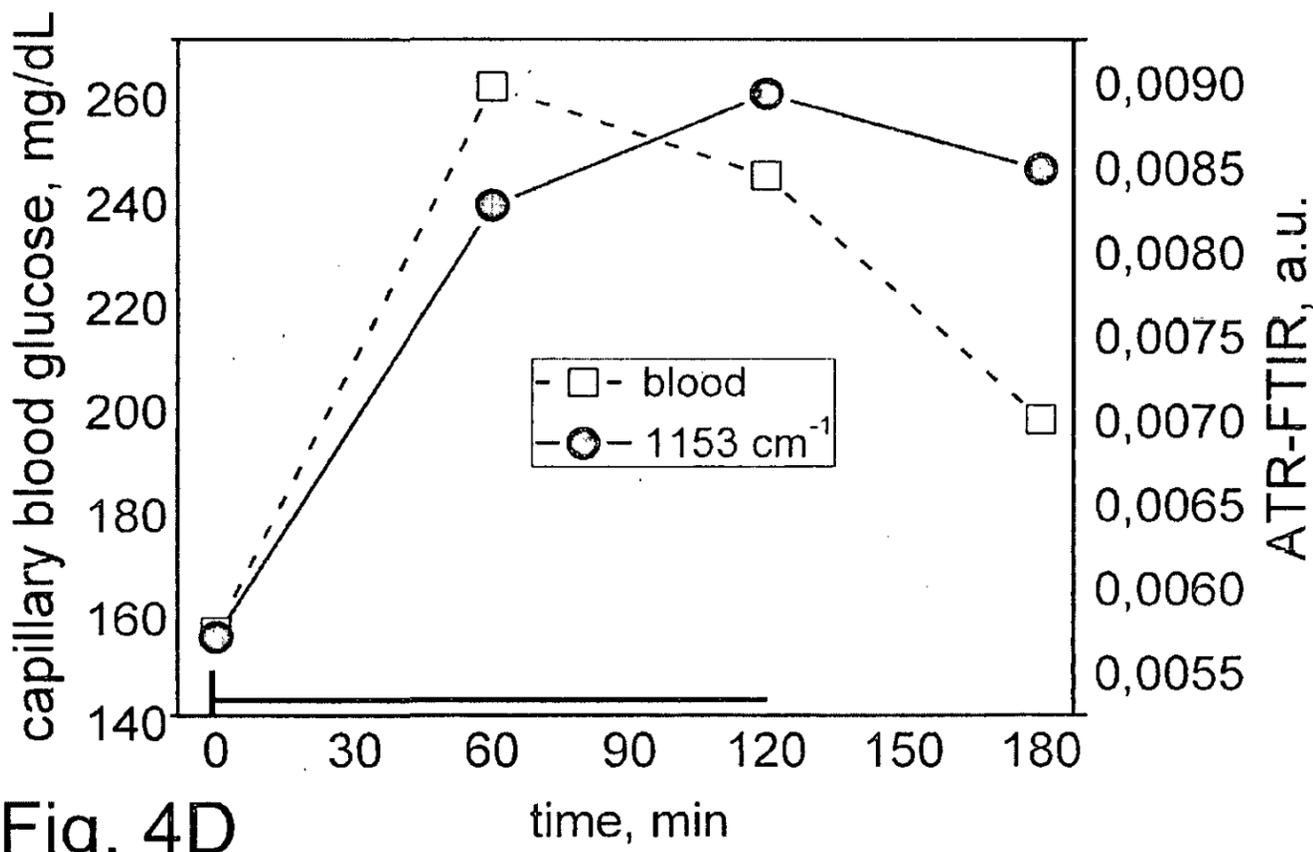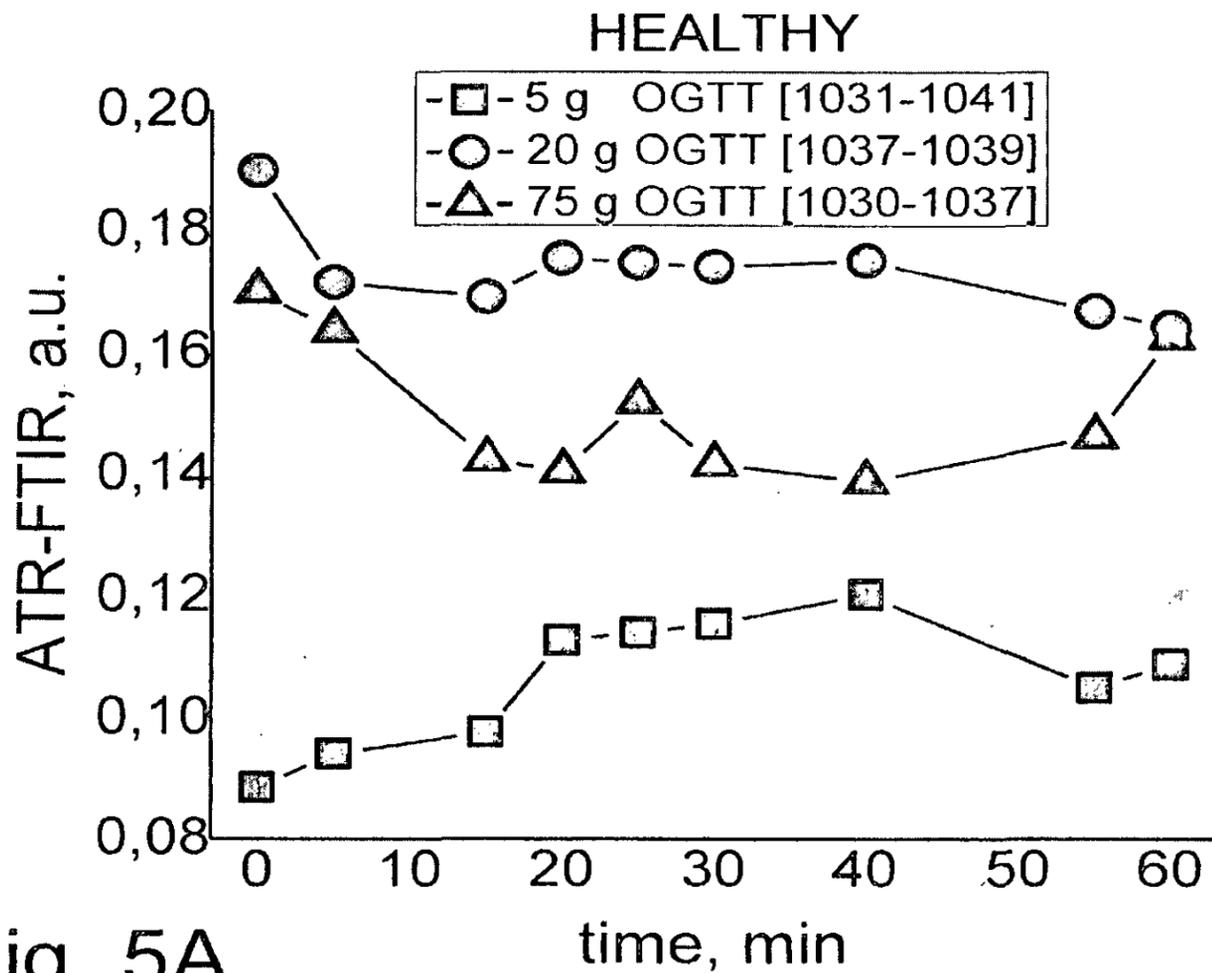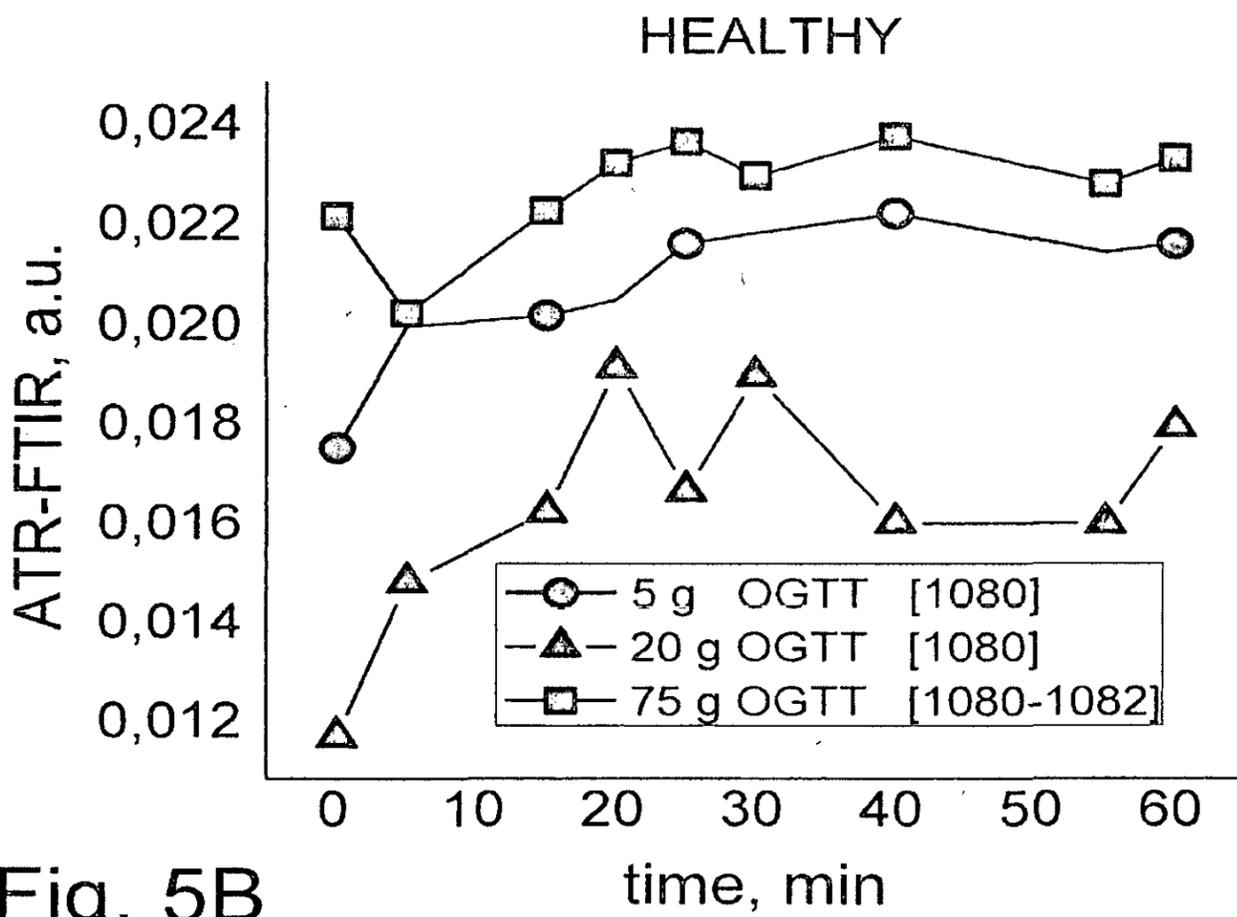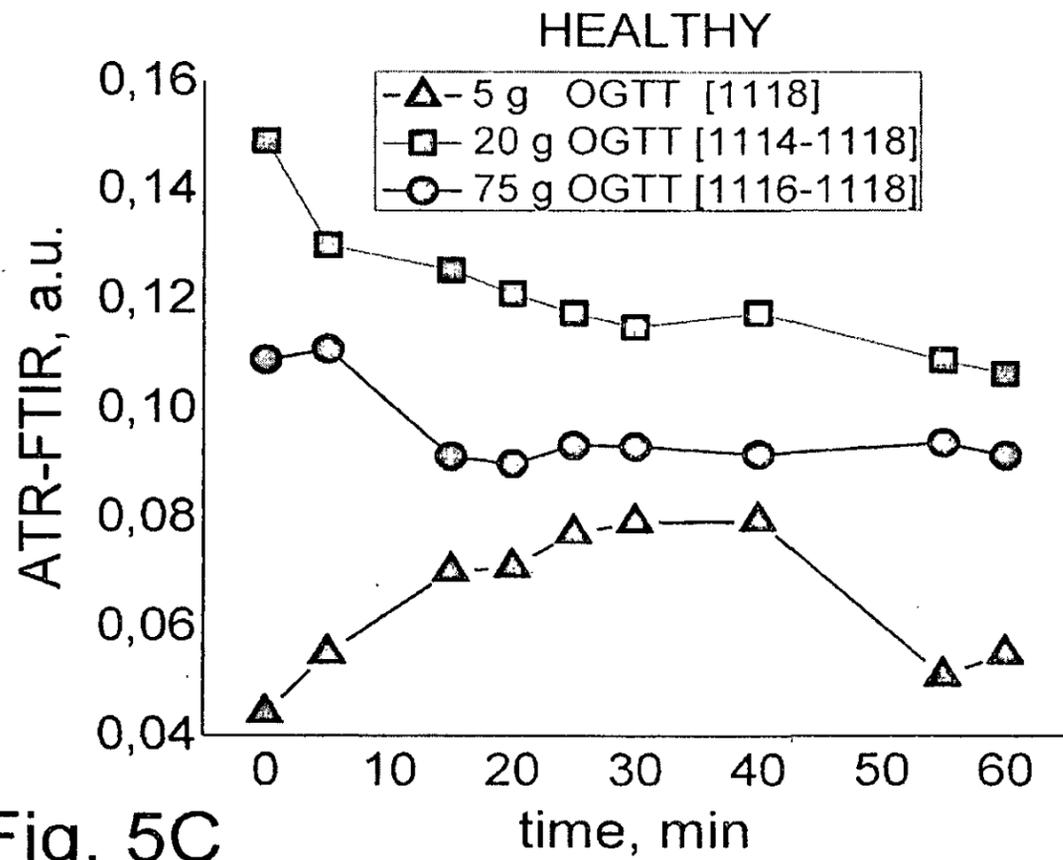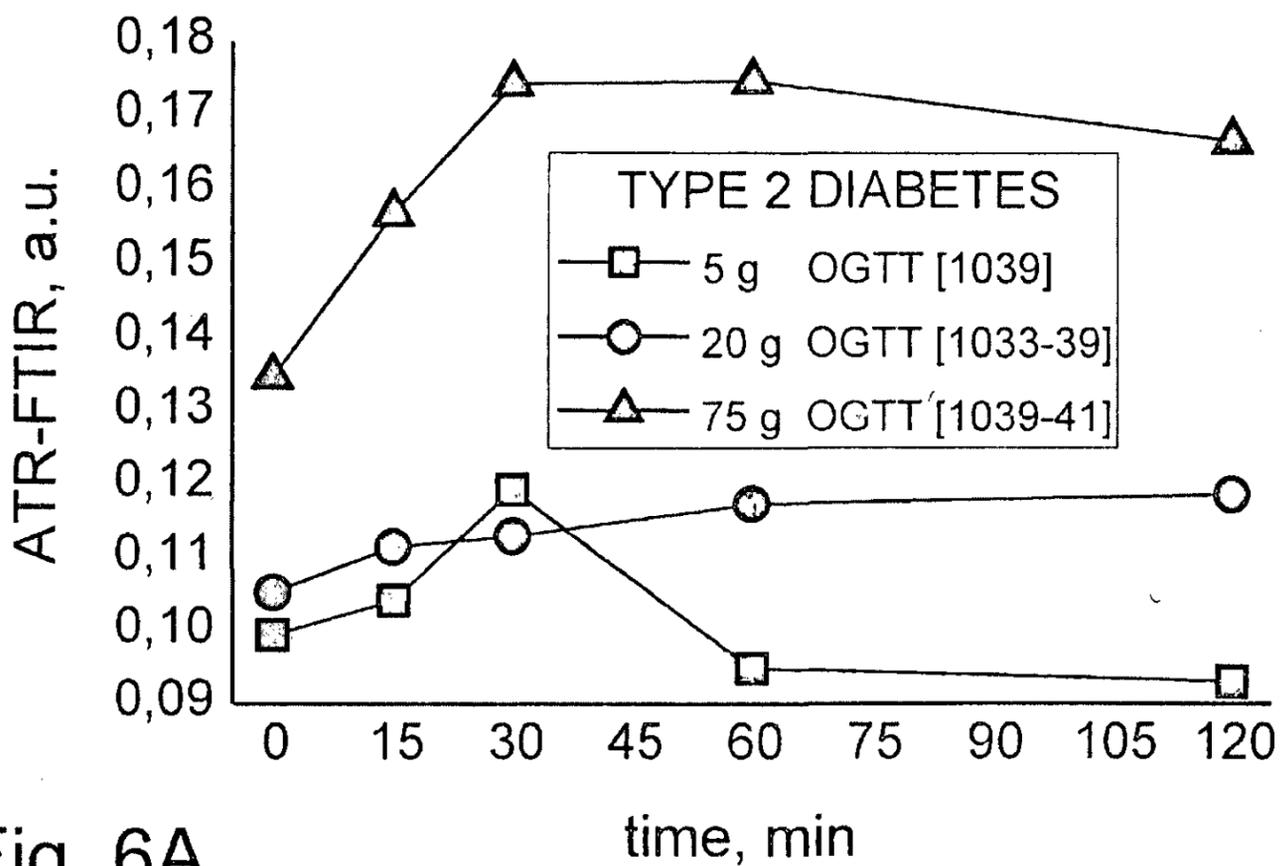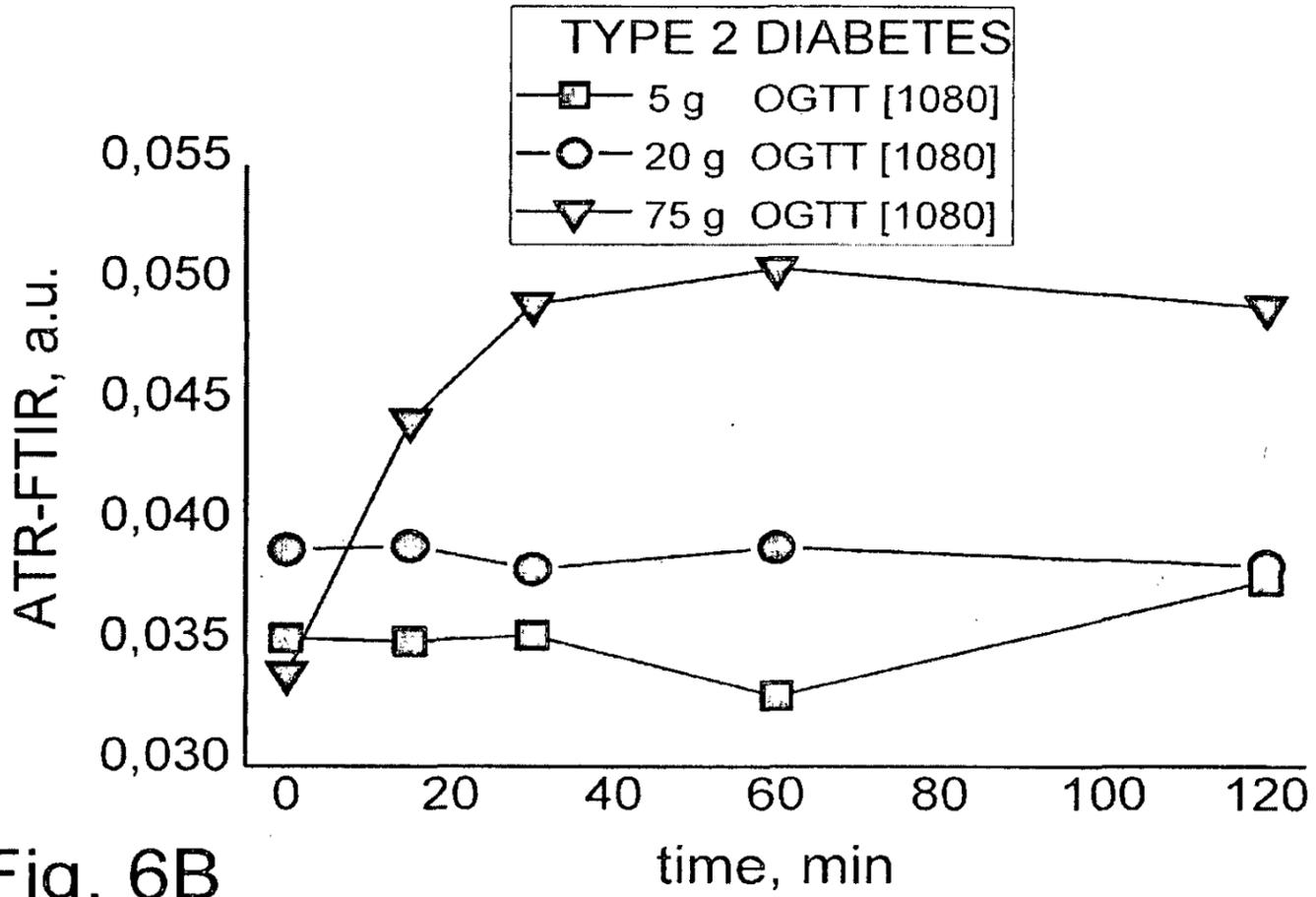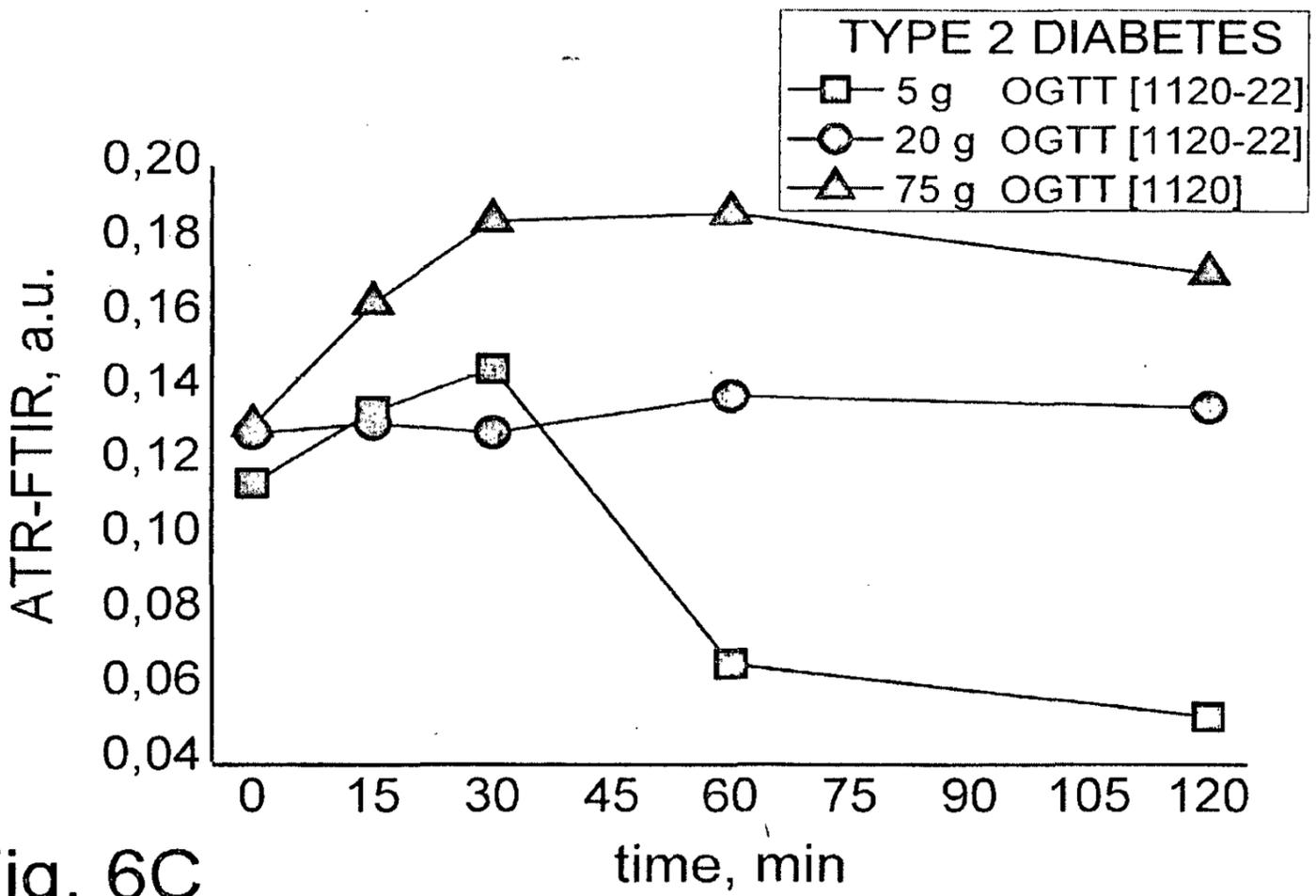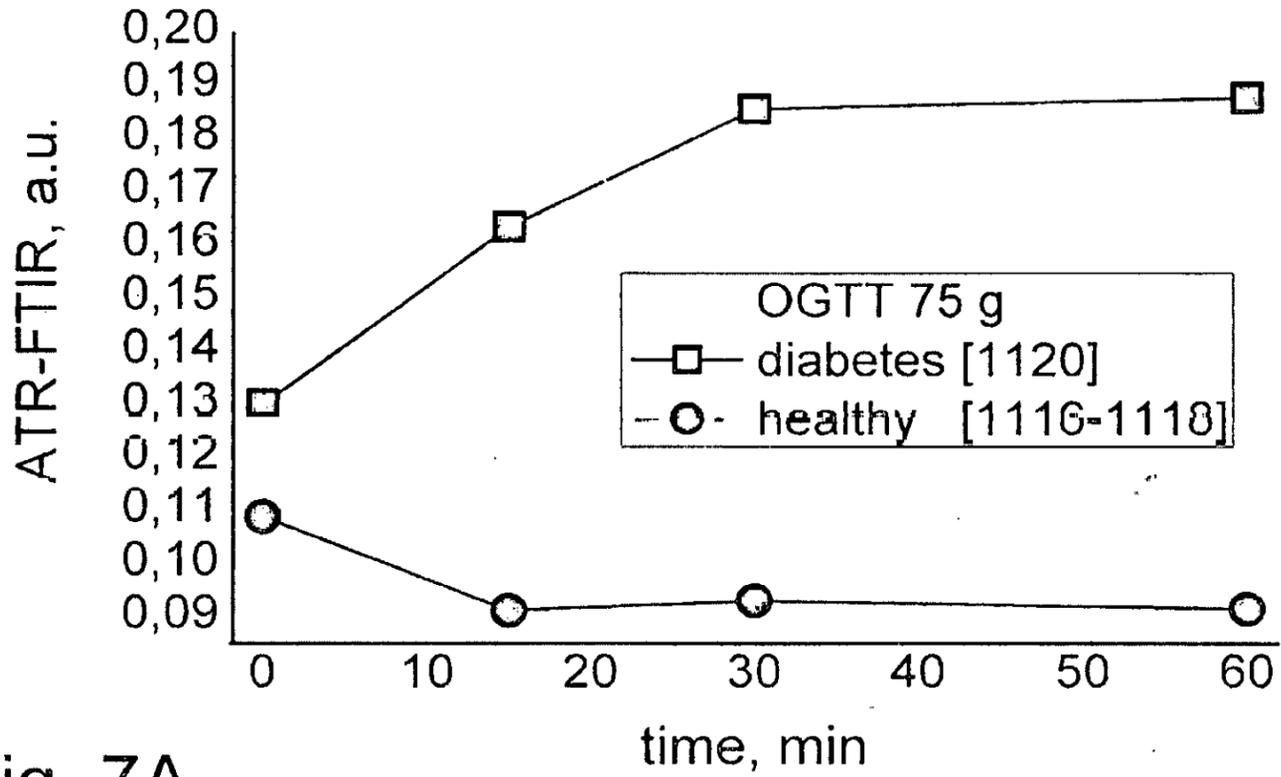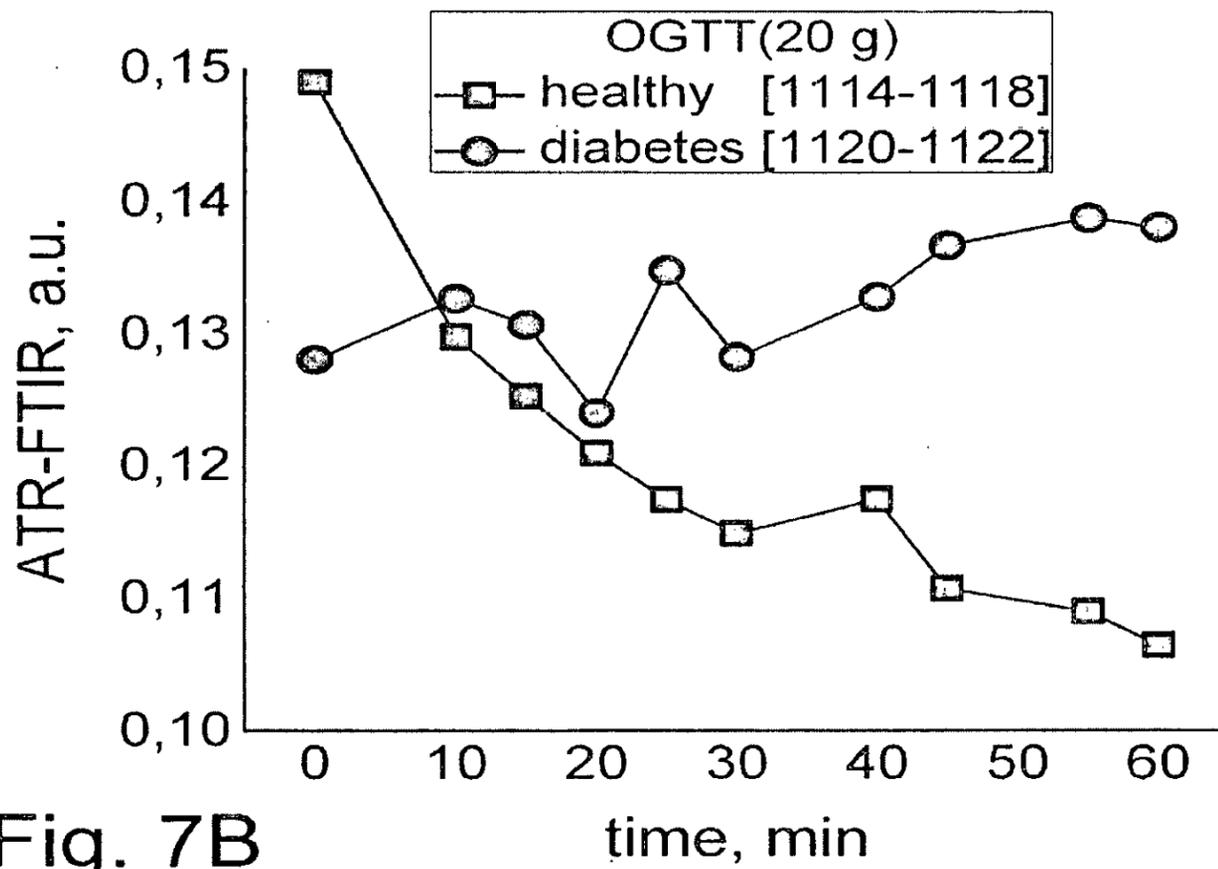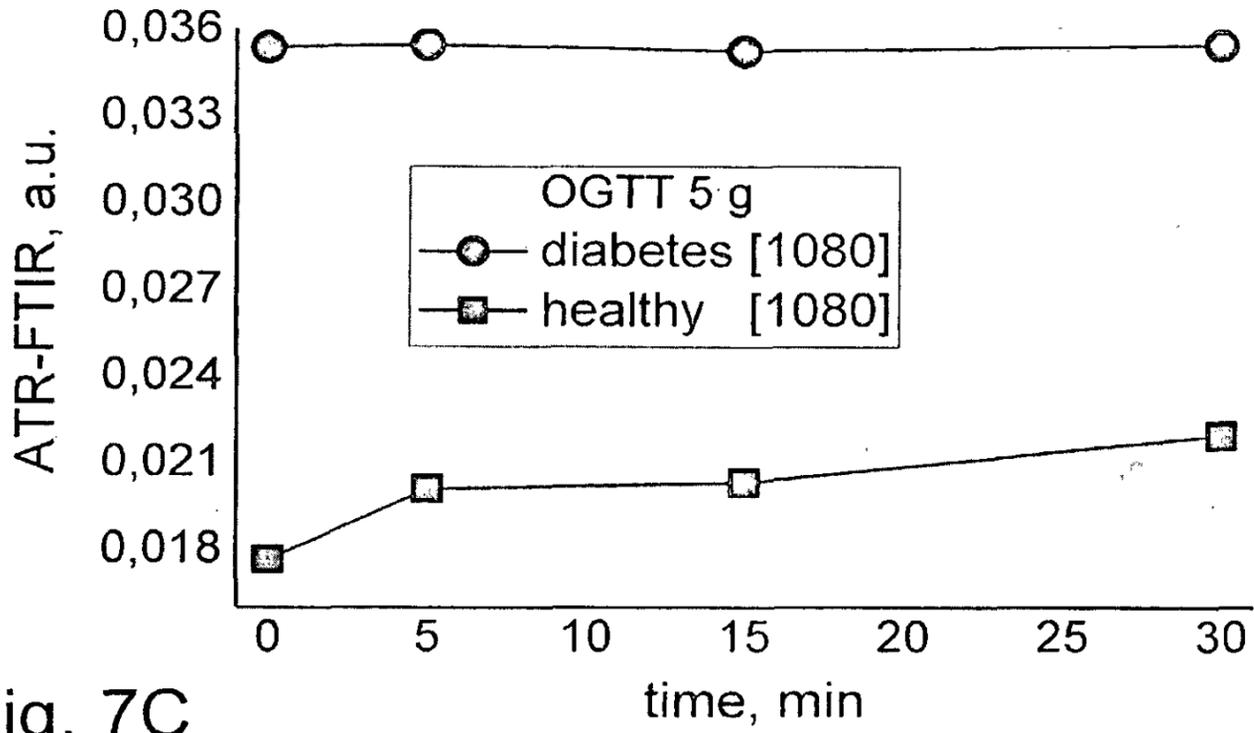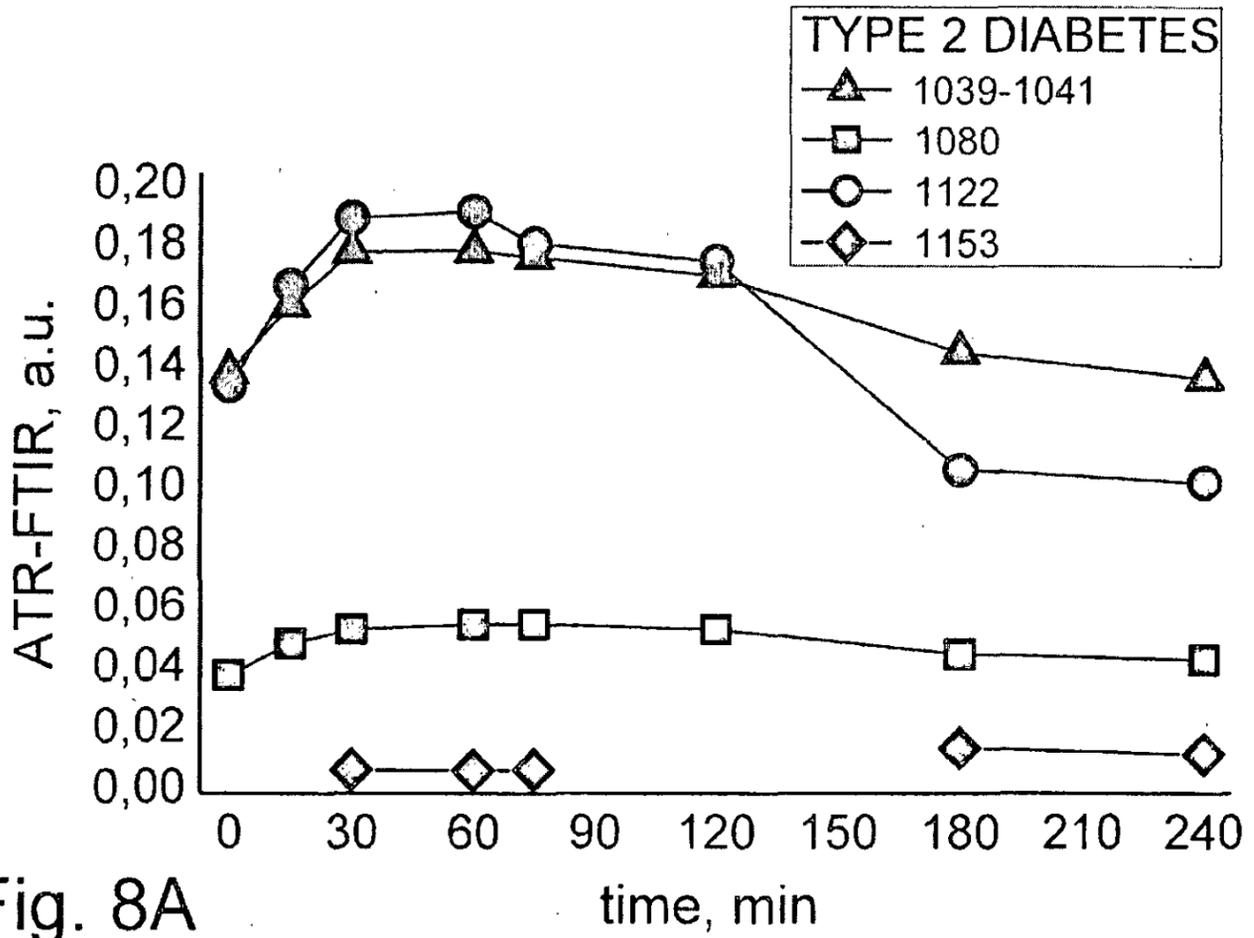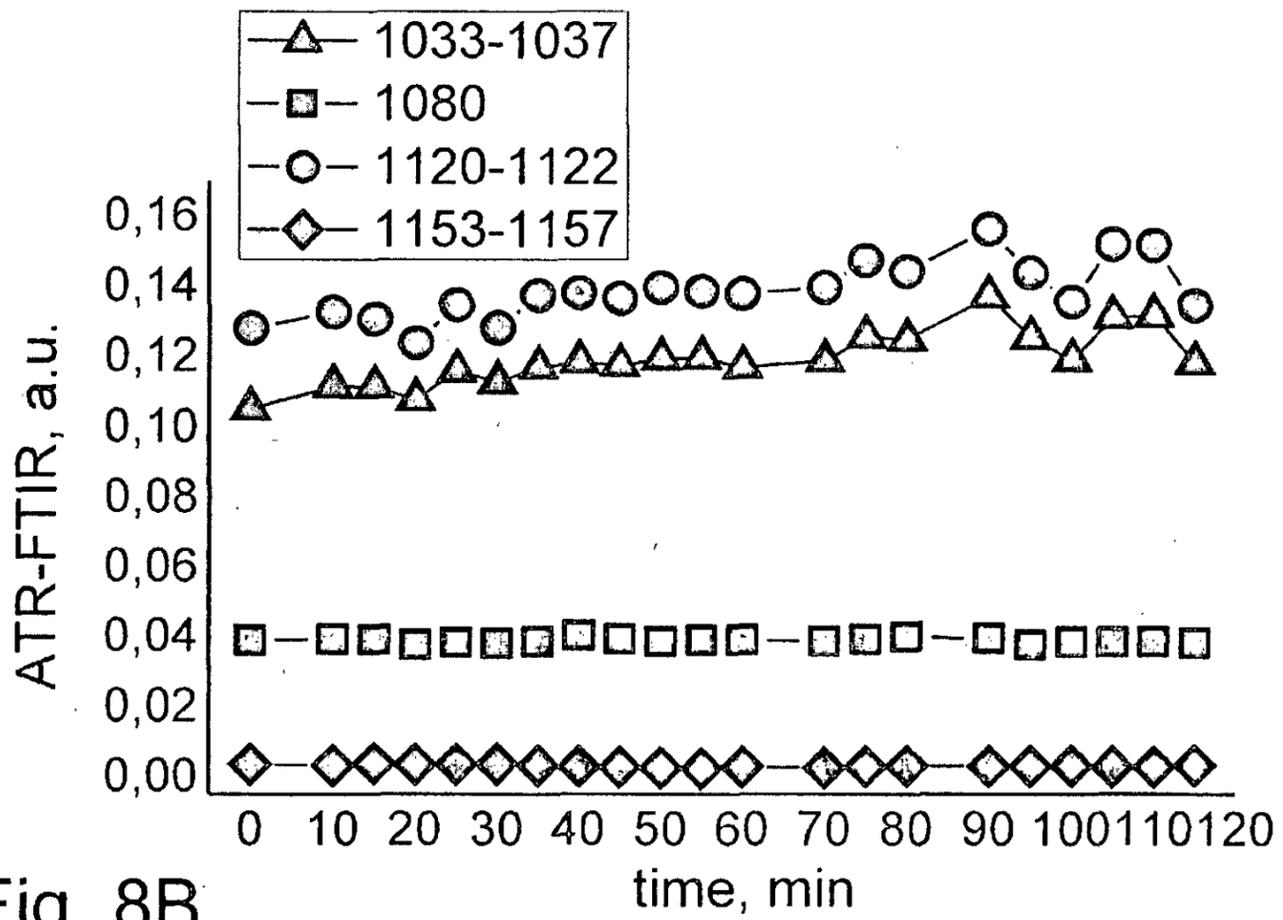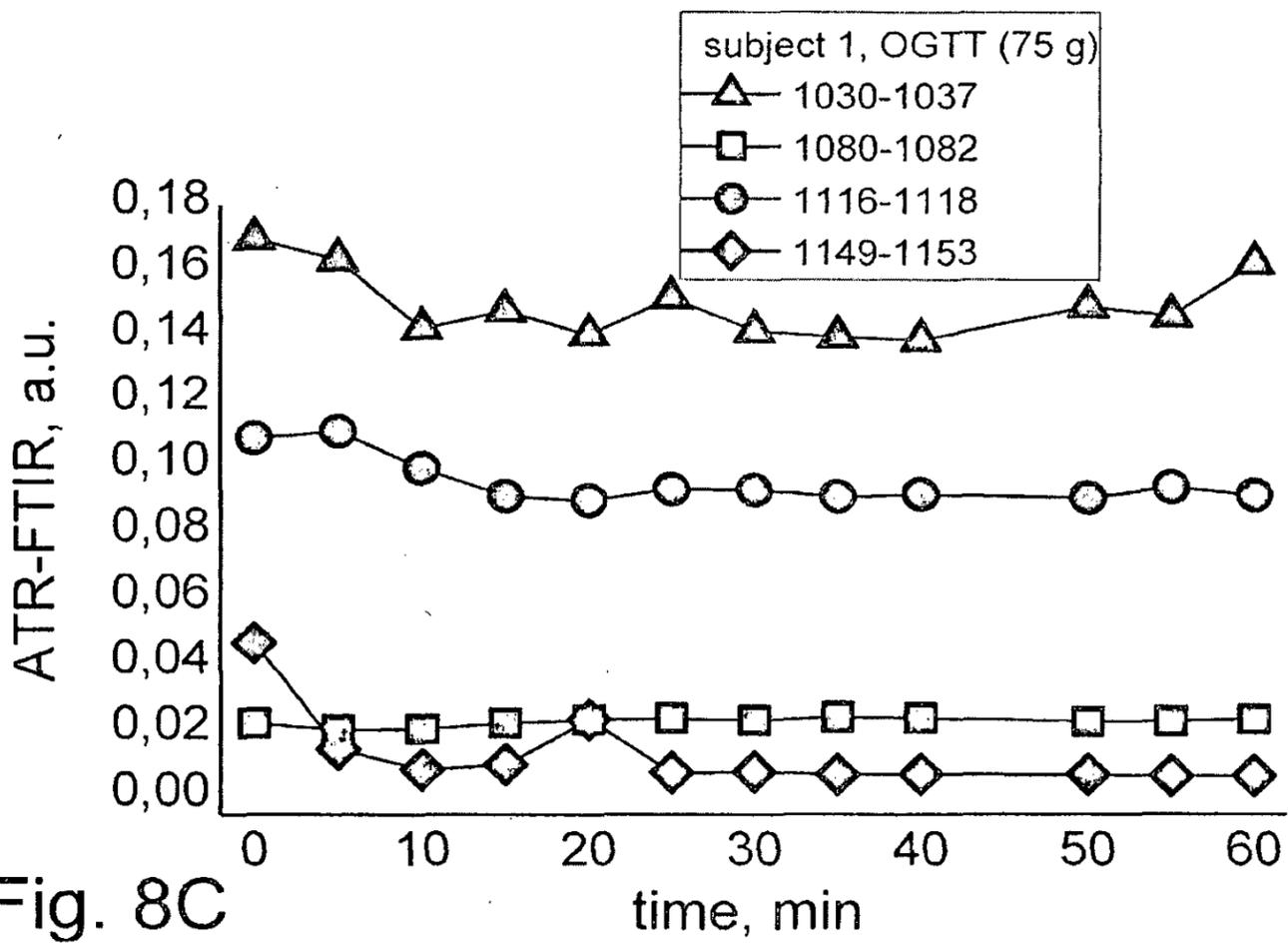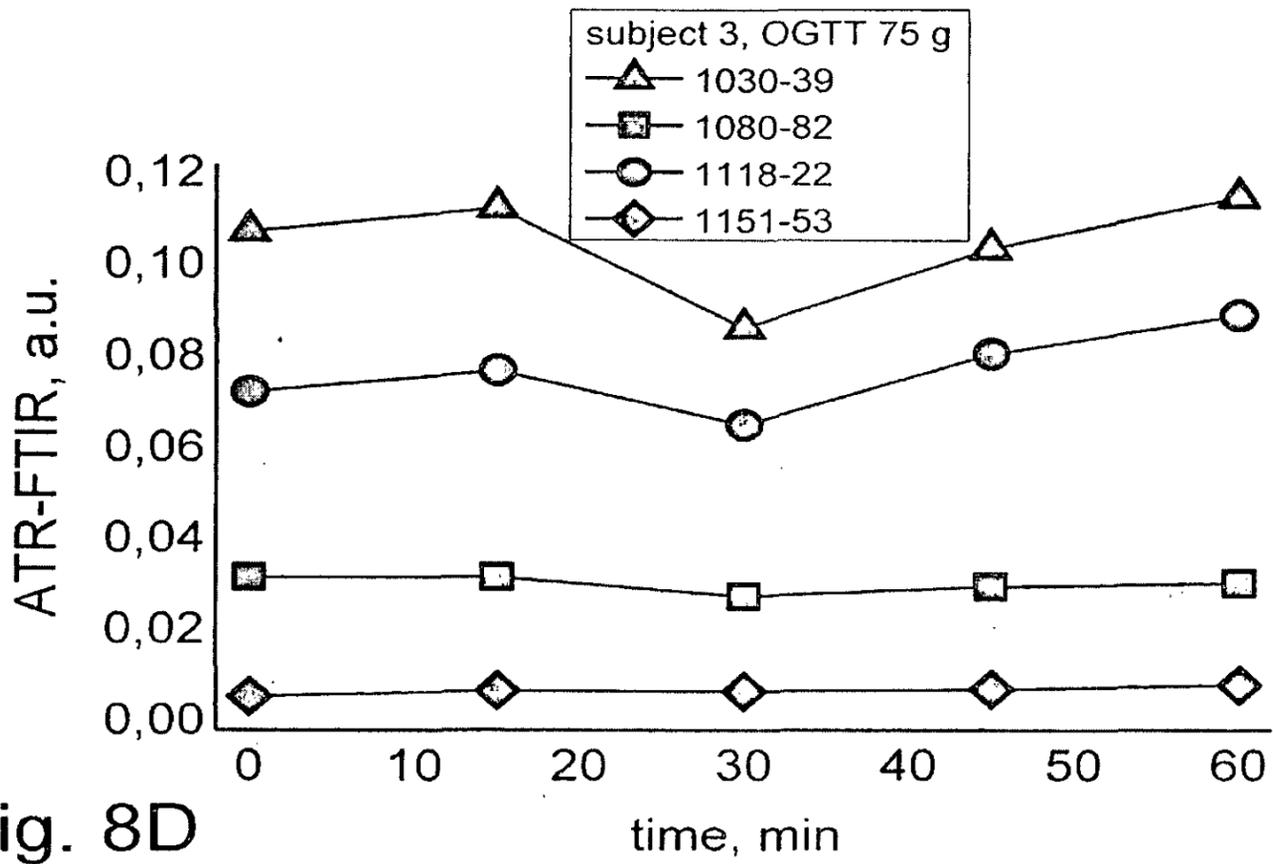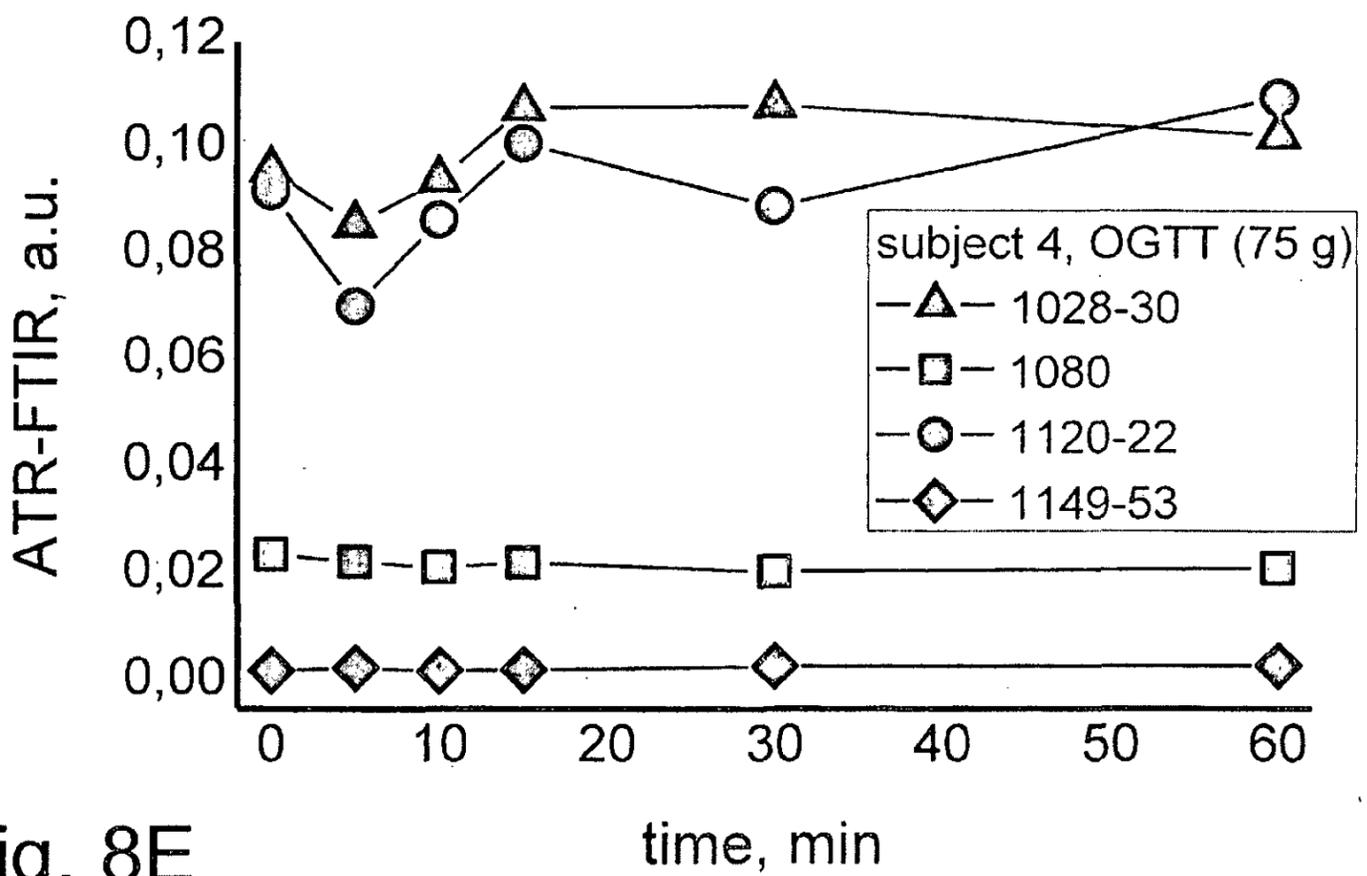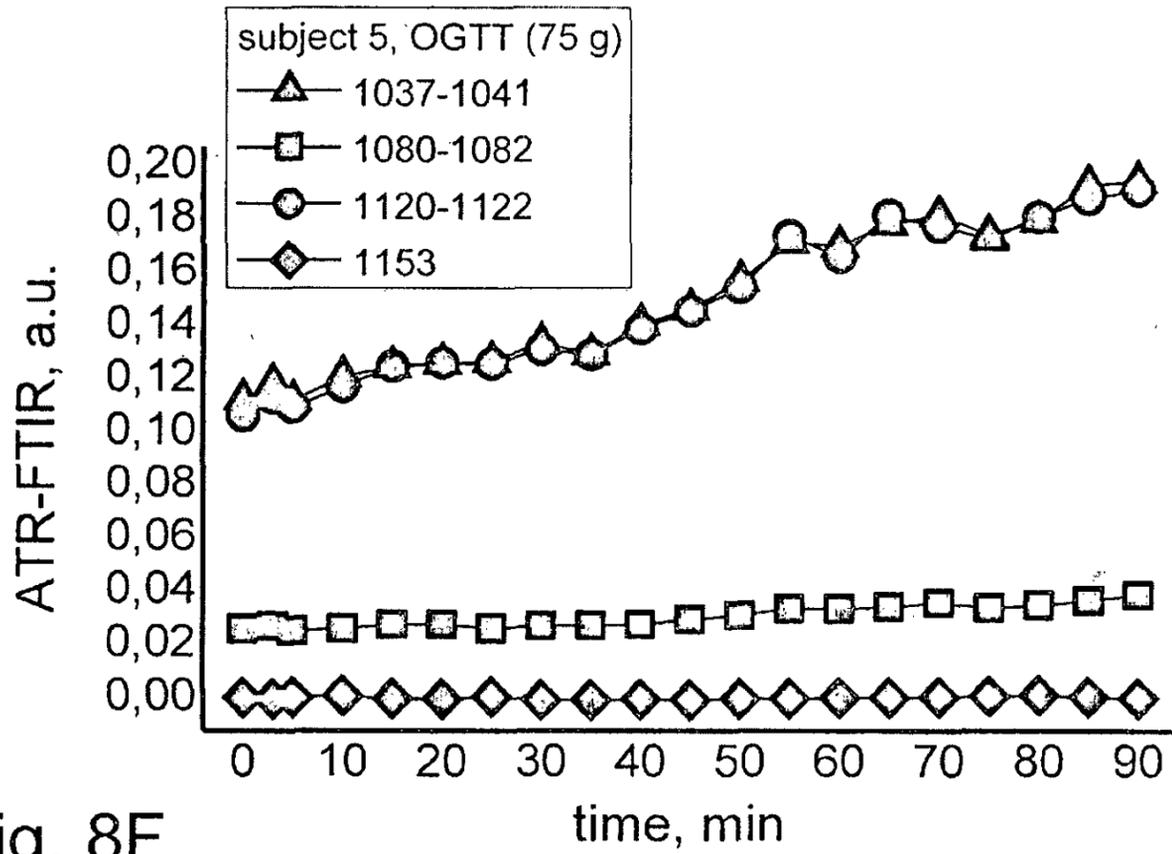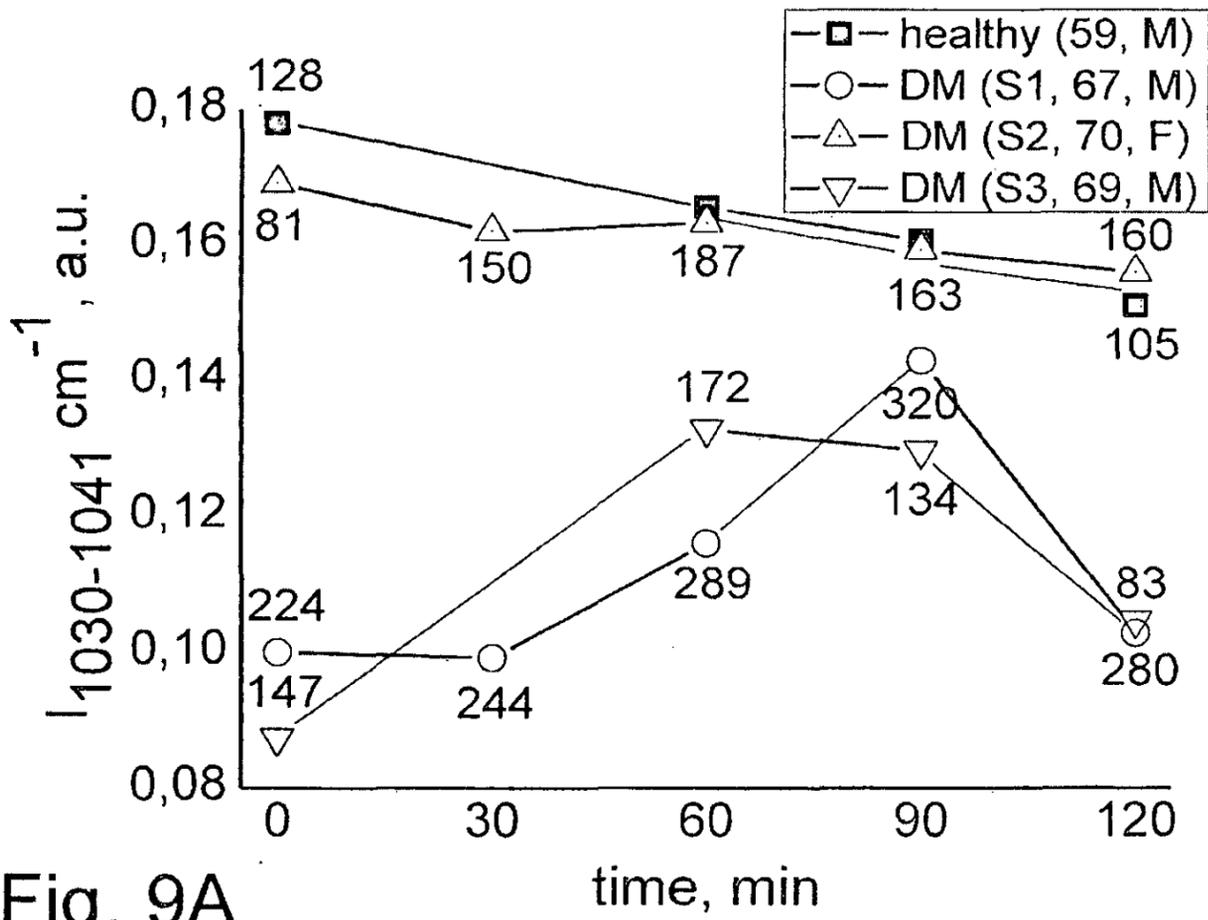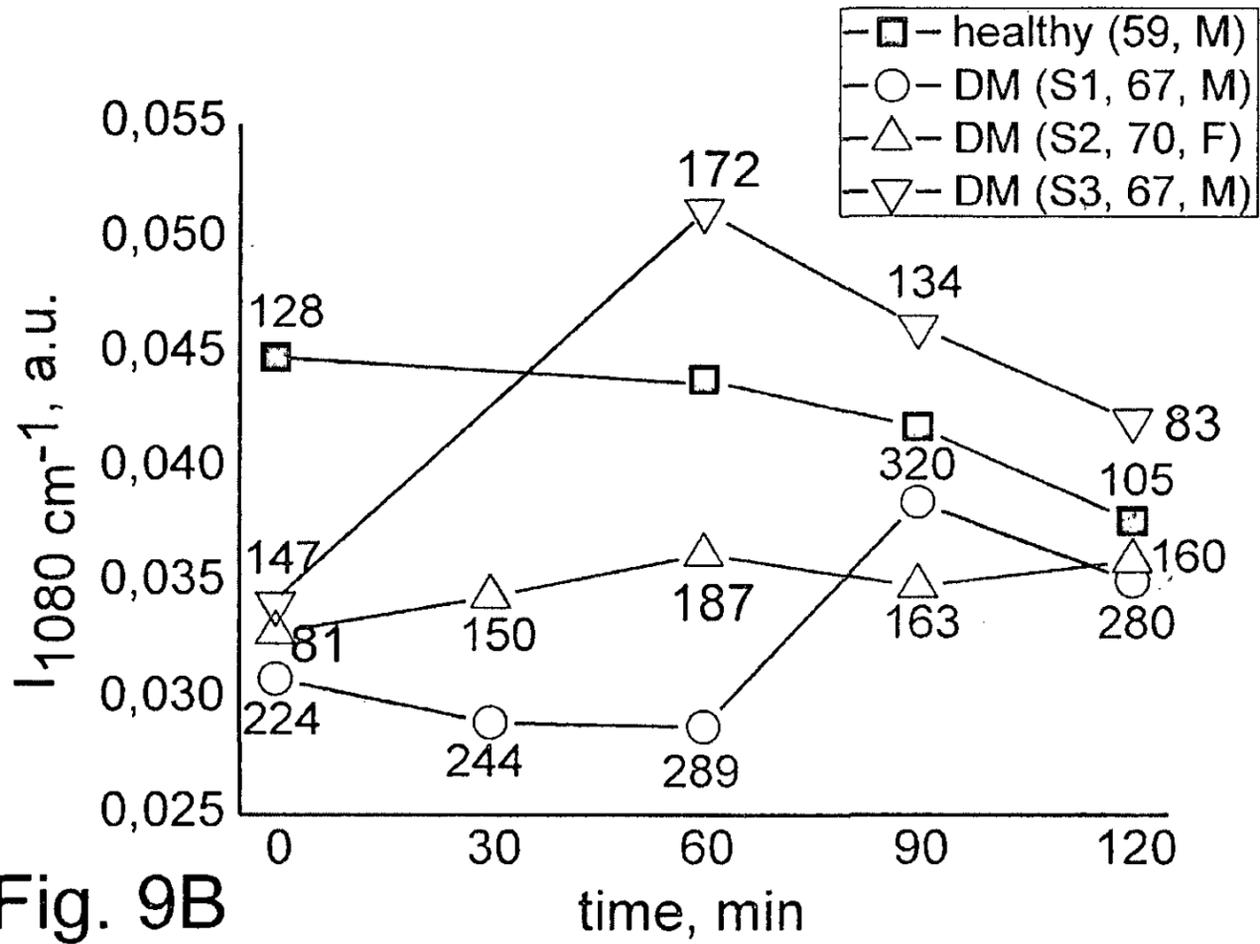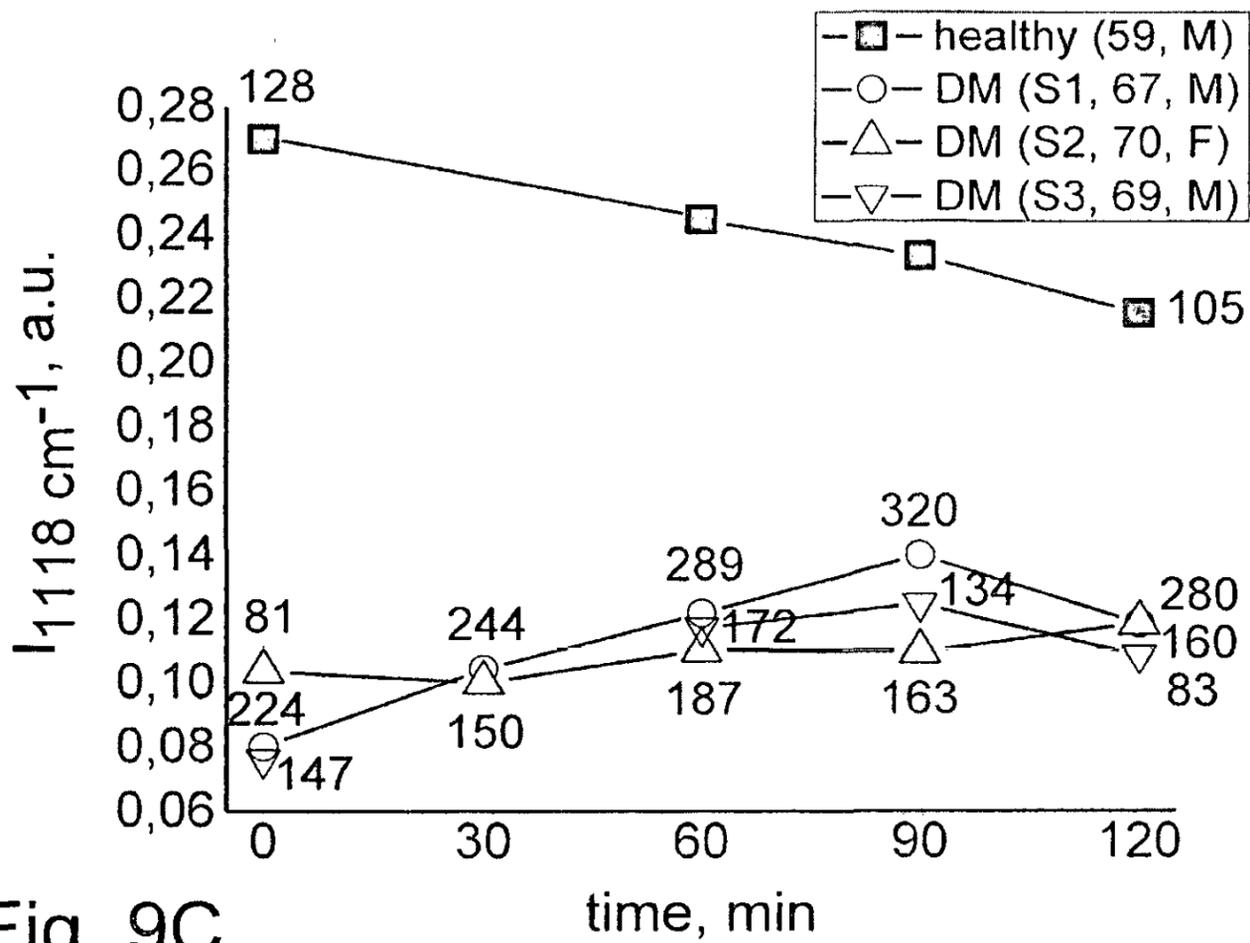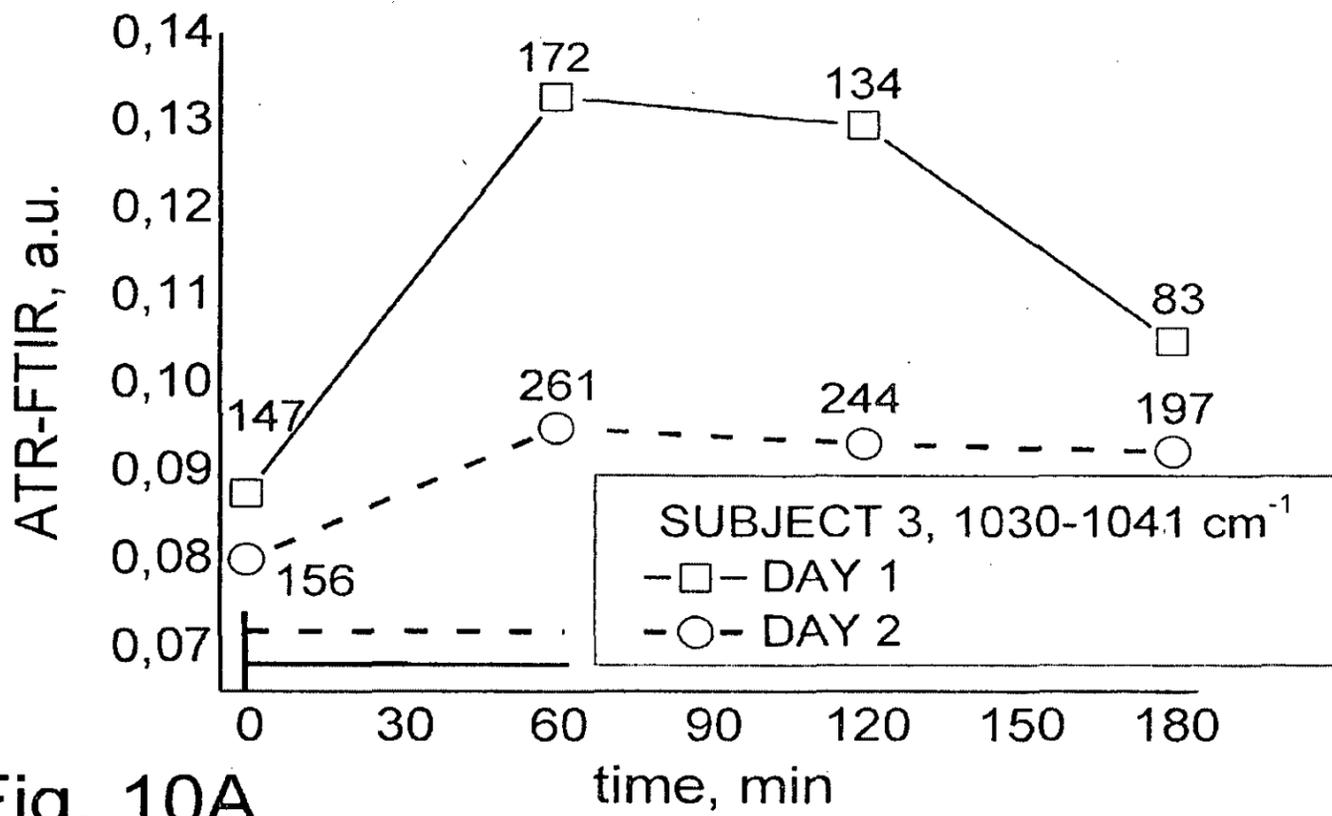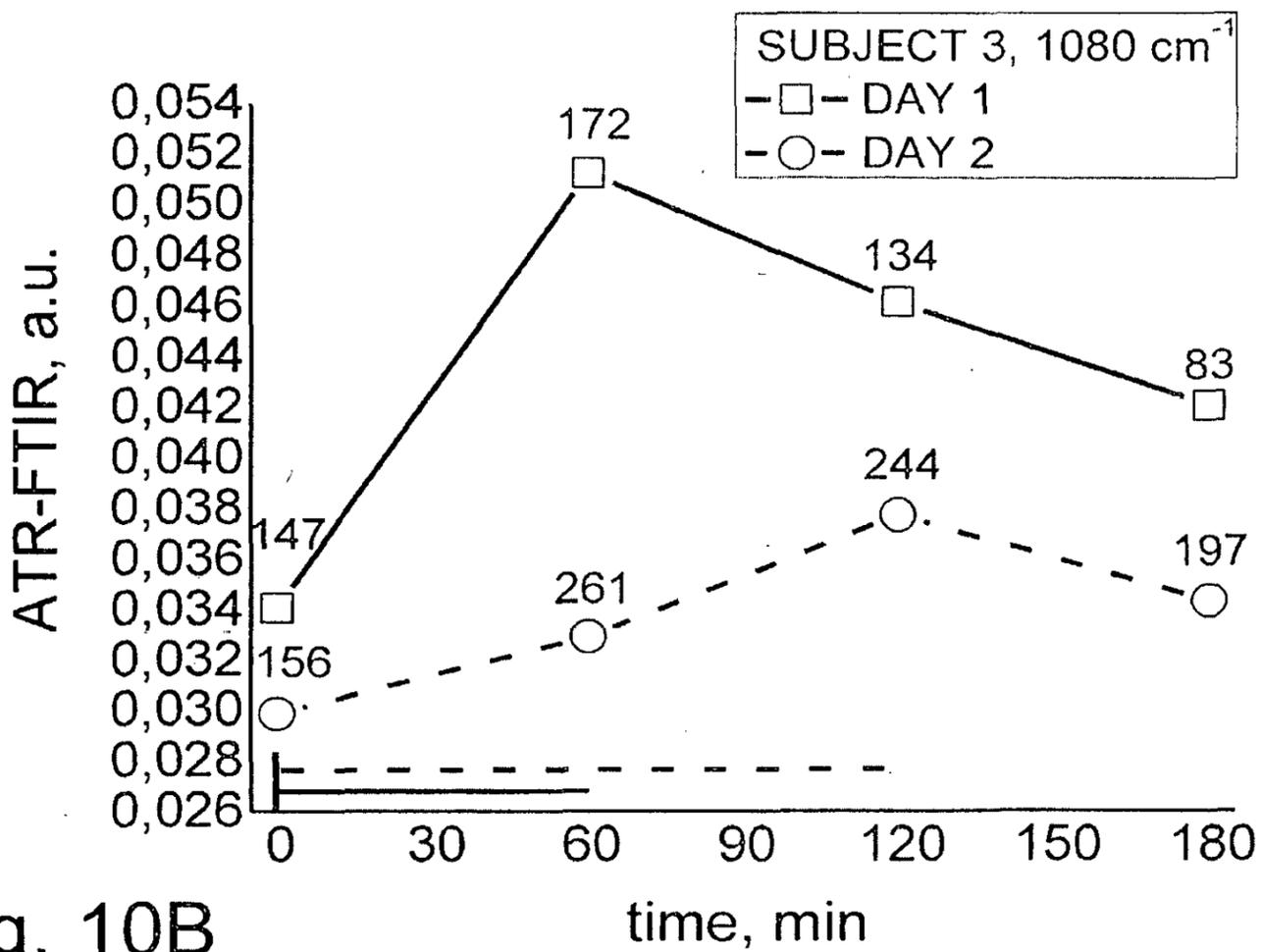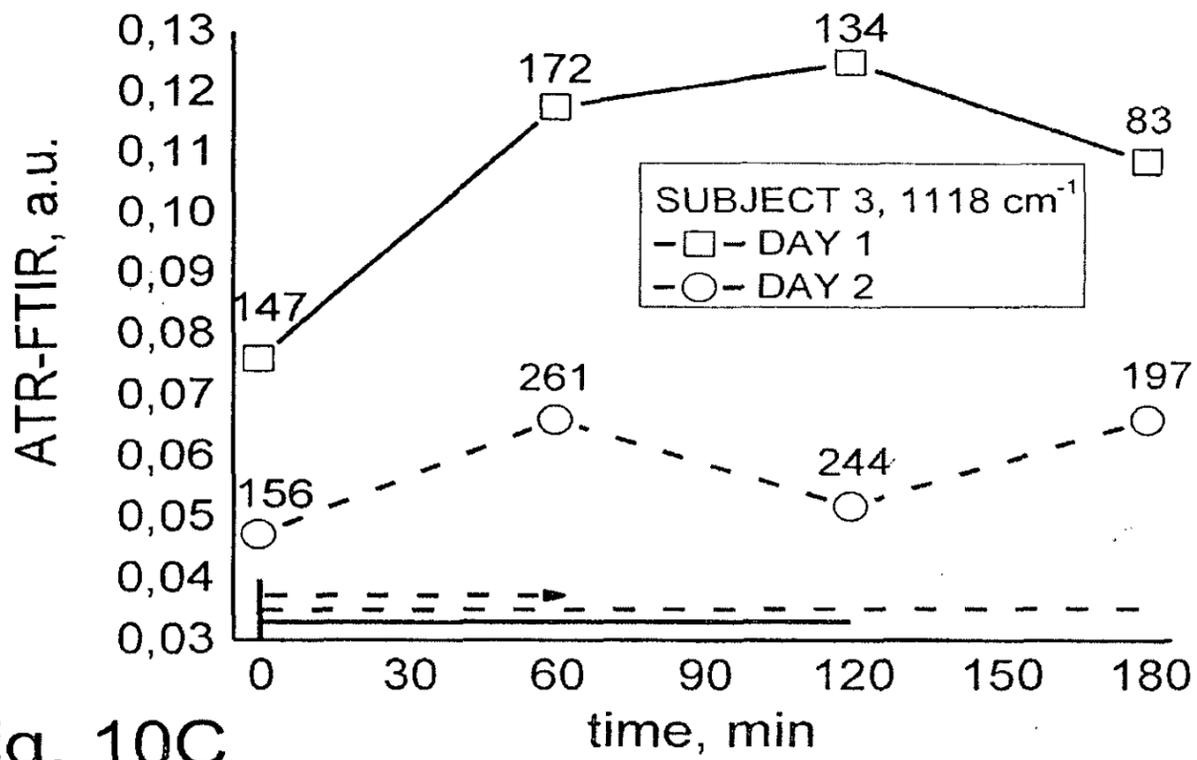
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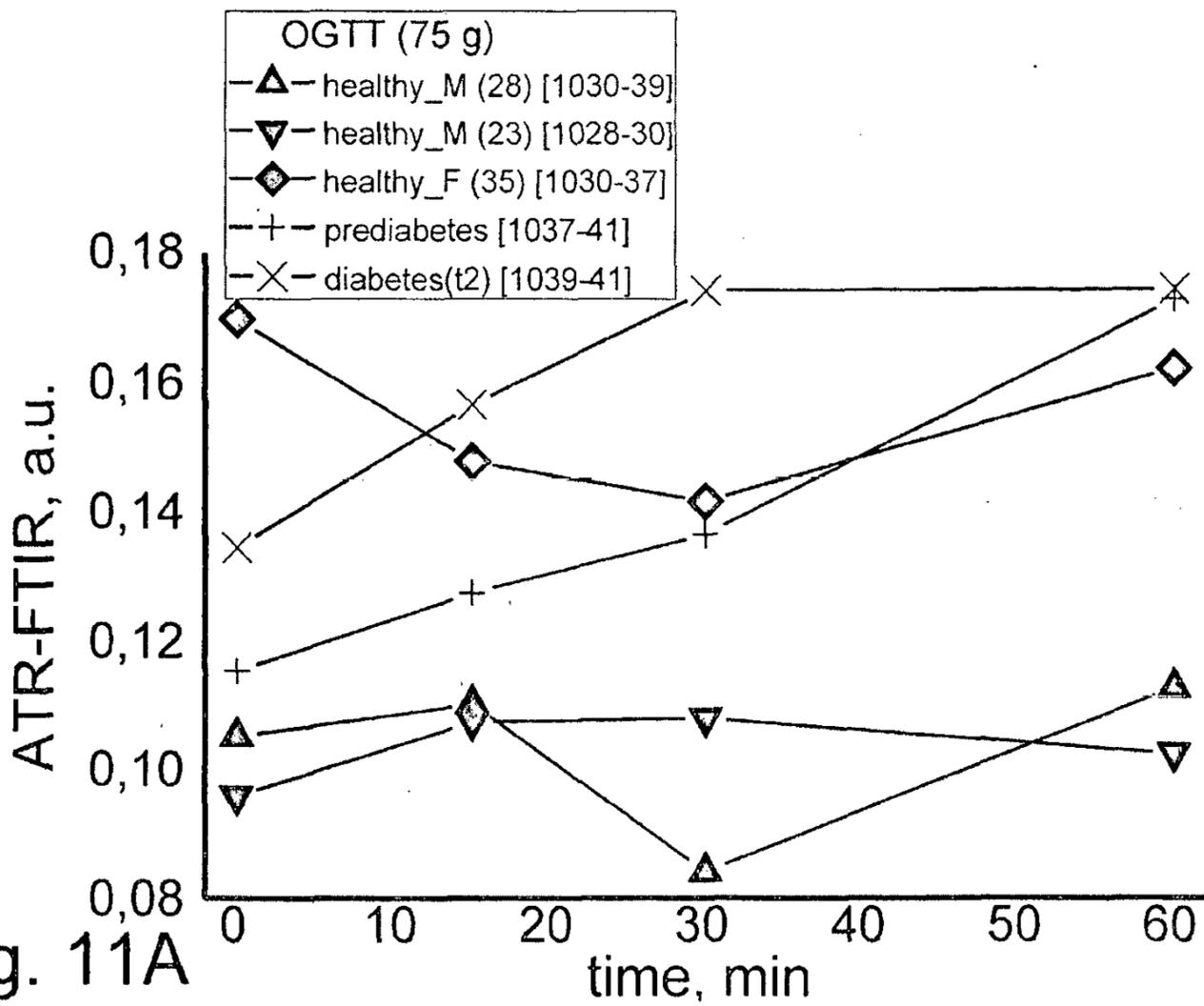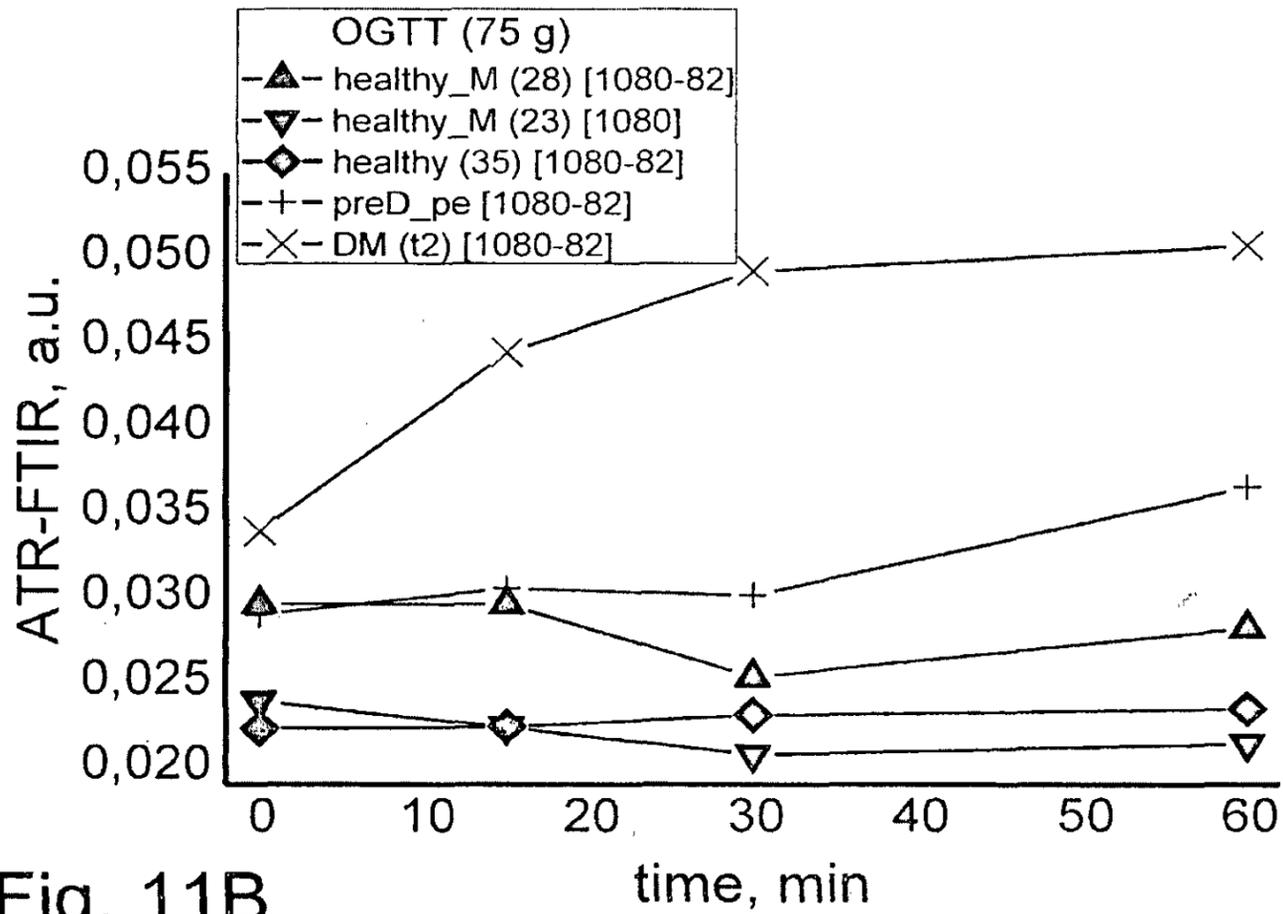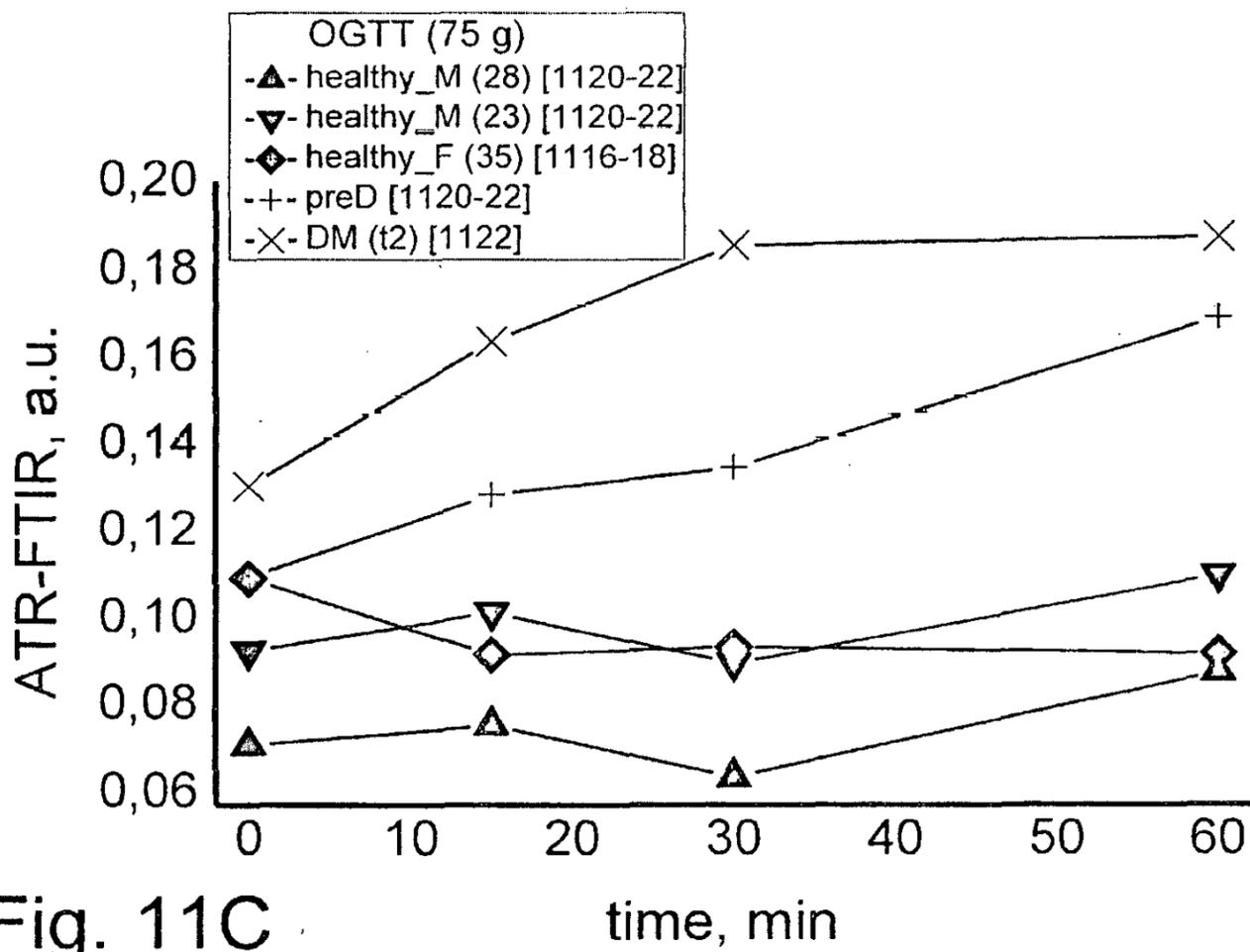
Fig. 11A

Fig. 11B

Fig. 11C
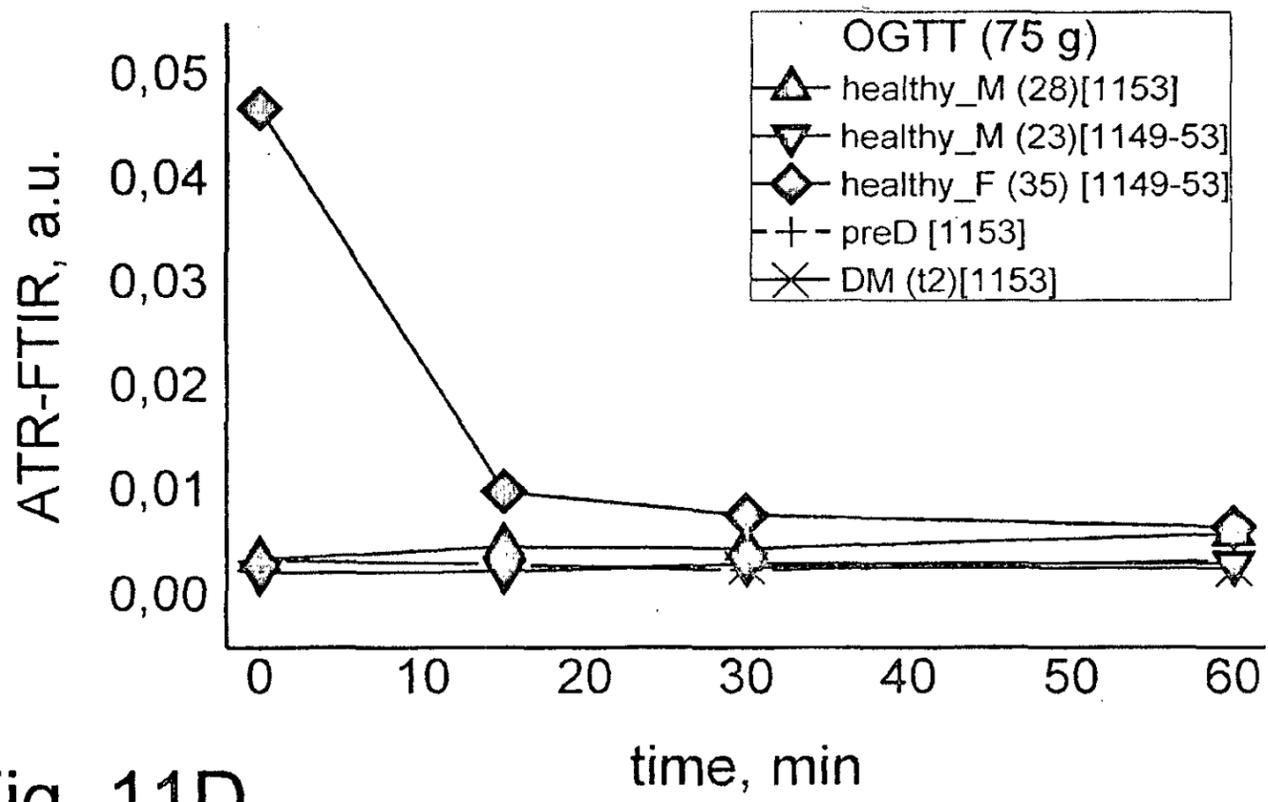
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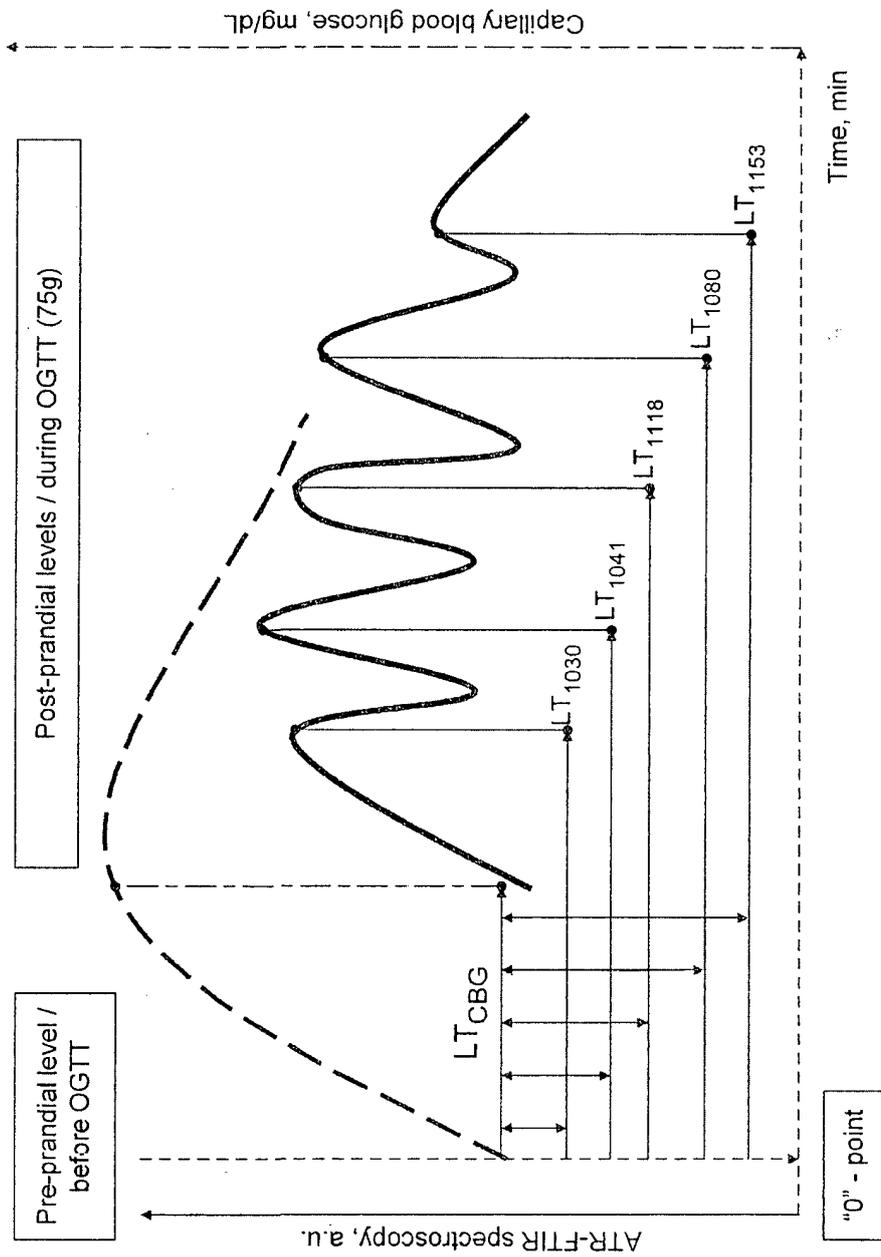
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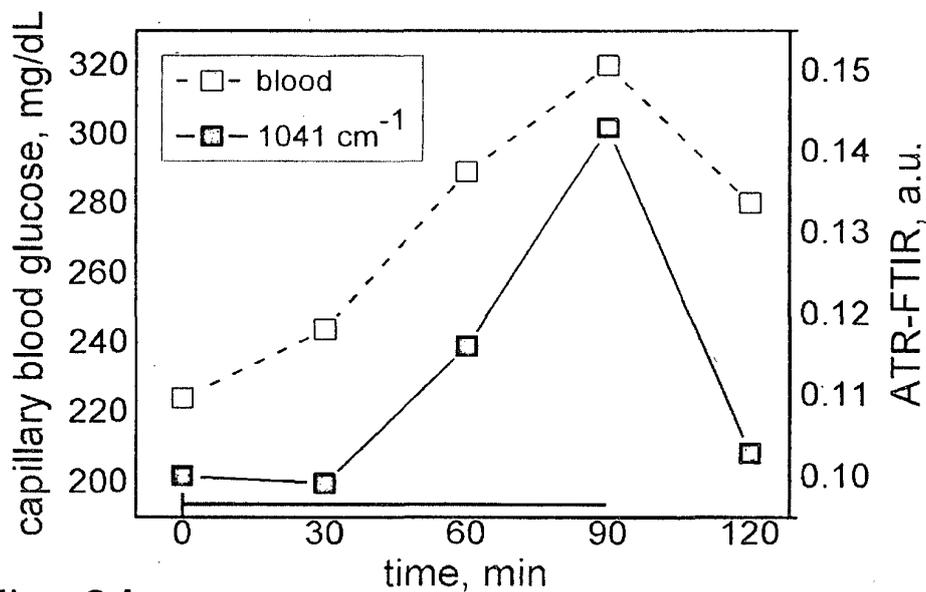
Fig. 2A

Fig. 2B

(TARUN GANDHI)

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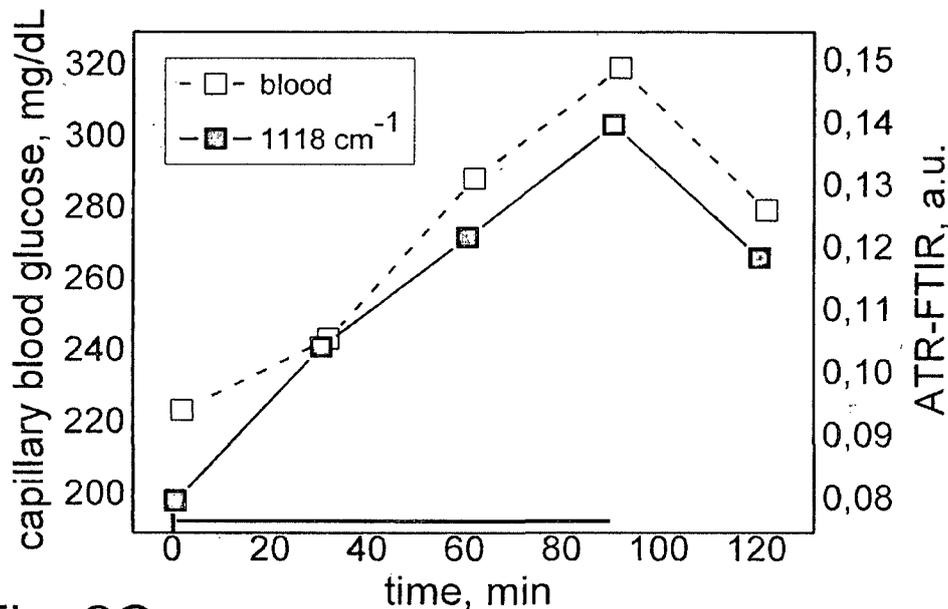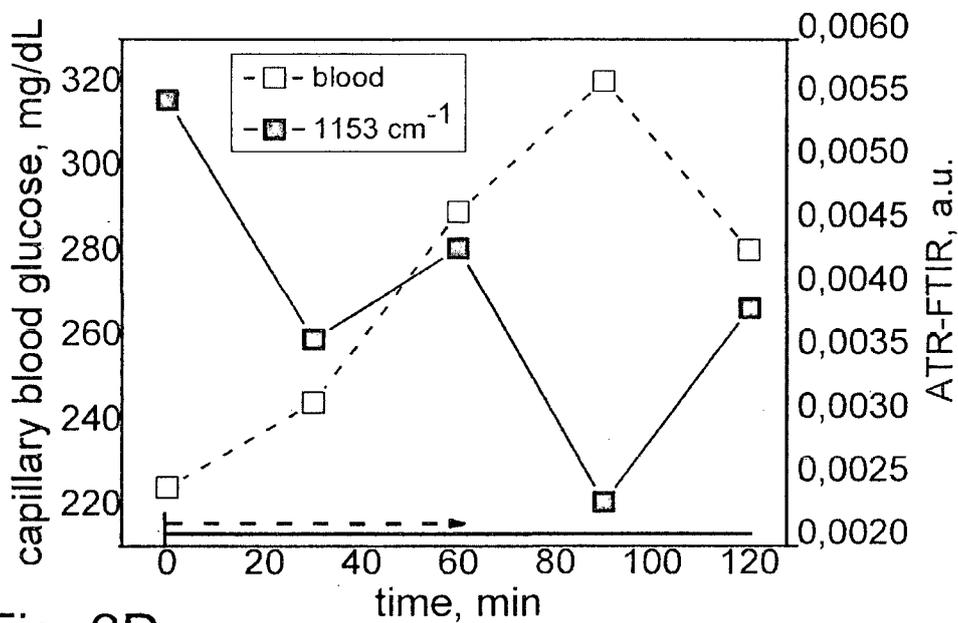
Fig. 2C

Fig. 2D

Fig. 3A

Fig. 3B

Fig. 3C

Fig. 3D

Fig. 4A

Fig. 4B

Fig.4C

Fig. 4D

HEALTHY

Legend:
-□- 5 g OGTT [1031-1041]
-○- 20 g OGTT [1037-1039]
-△- 75 g OGTT [1030-1037]

Fig. 5A

HEALTHY

Legend:
—○— 5 g OGTT [1080]
—△— 20 g OGTT [1080]
—□— 75 g OGTT [1080-1082]

Fig. 5B

(TARUN GANDHI)

PATENT AGENT [IN/PA-1740]

HEALTHY

-△- 5 g   OGTT [1118]
-□- 20 g OGTT [1114-1118]
-○- 75 g OGTT [1116-1118]

Fig. 5C

time, min

TYPE 2 DIABETES

-□- 5 g   OGTT [1039]
-○- 20 g OGTT [1033-39]
-△- 75 g OGTT [1039-41]

Fig. 6A

time, min
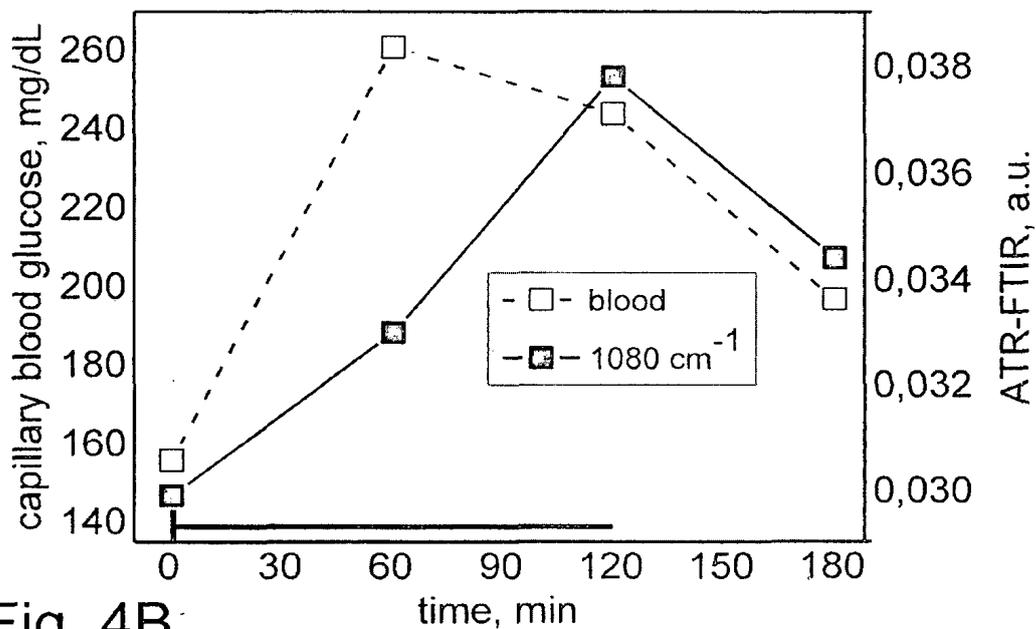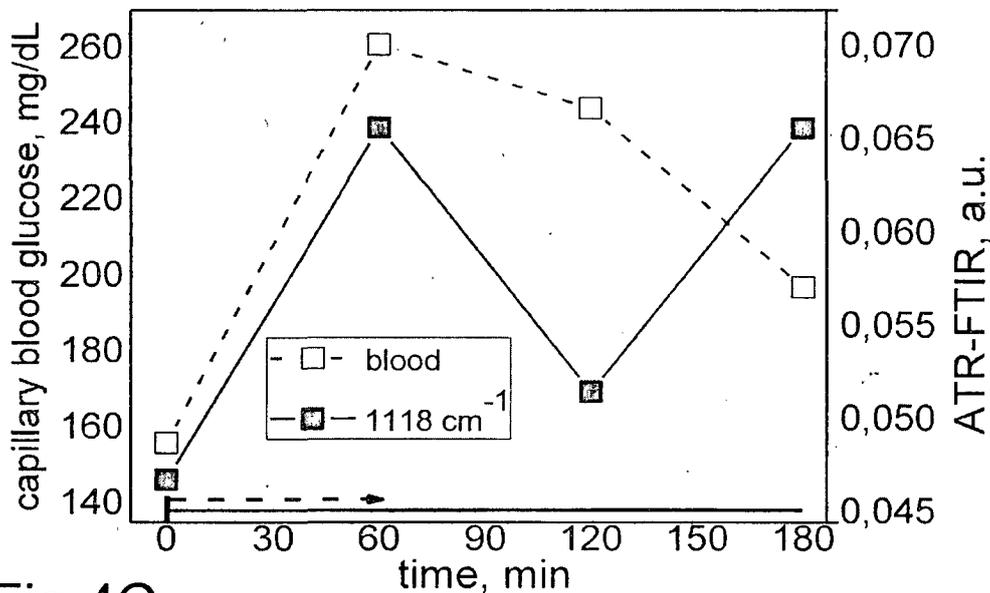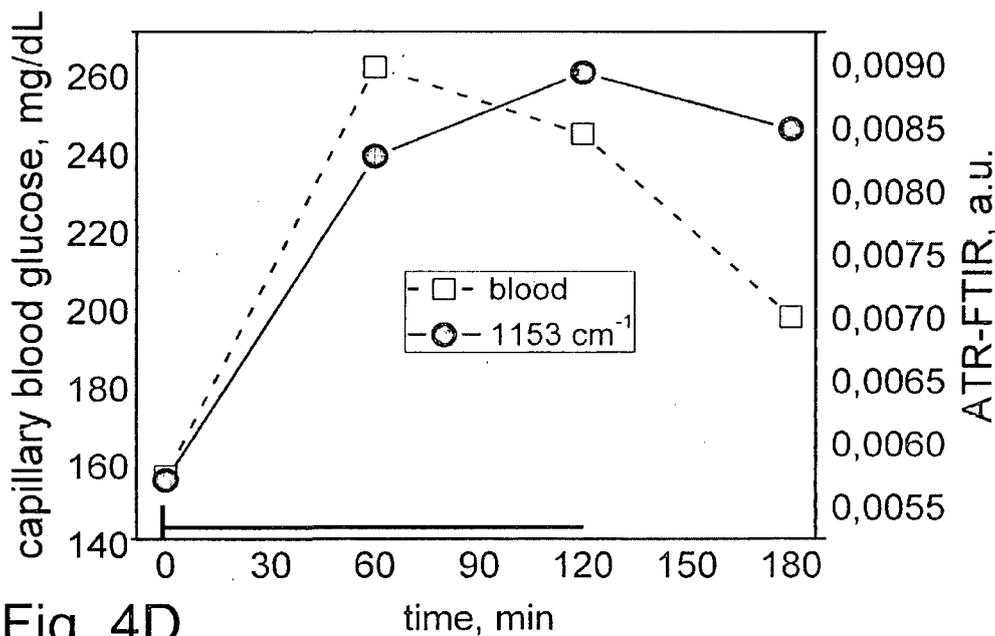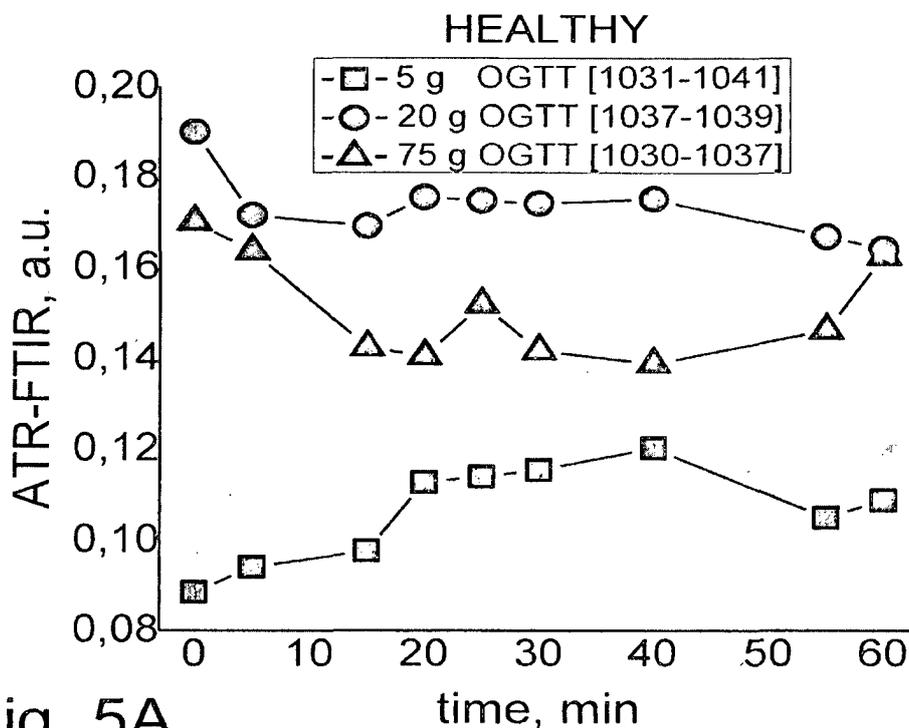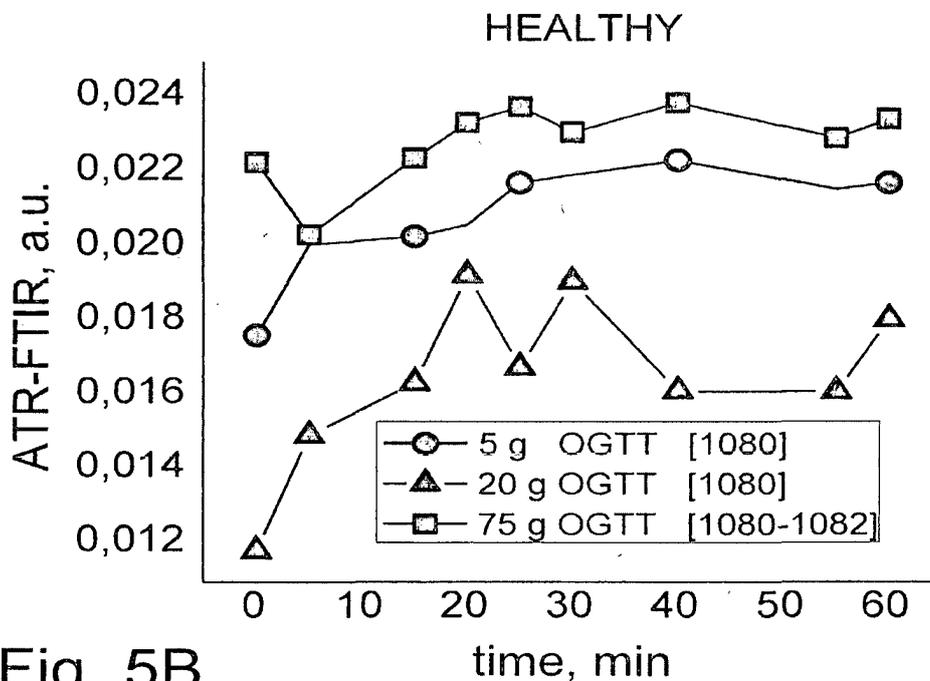
(TARUN GANDHI)

PATENT AGENT [IN/PA-1740]

Fig. 6B
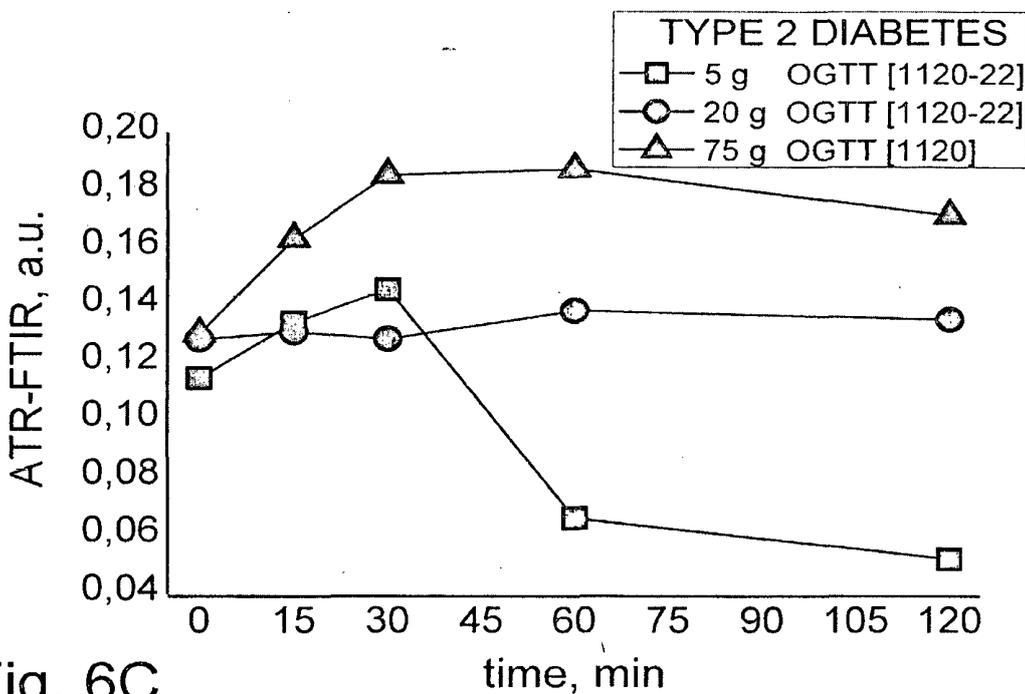
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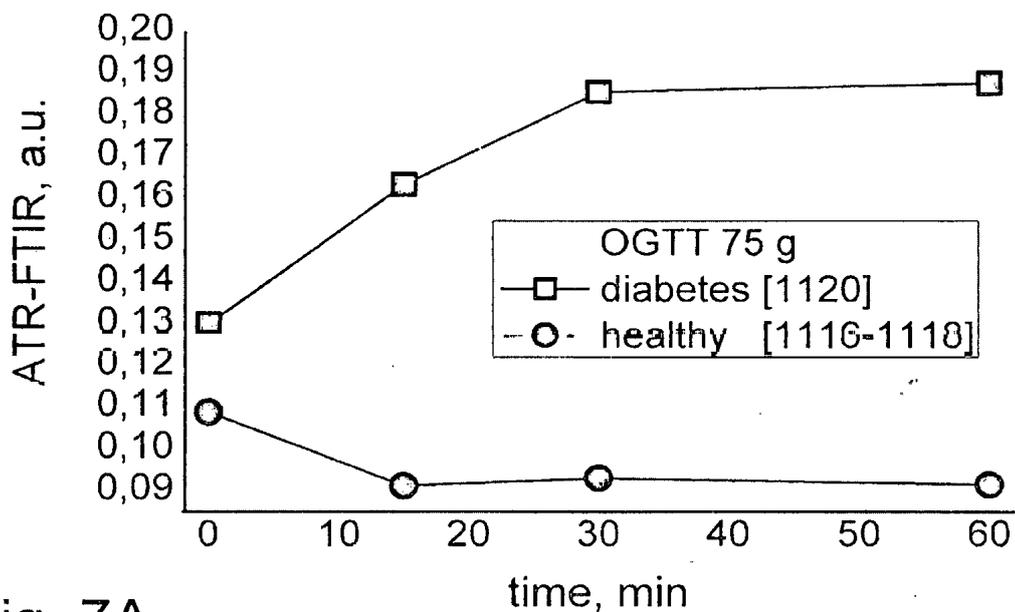
Fig. 7A

Fig. 7B

(TARUN GANDHI)
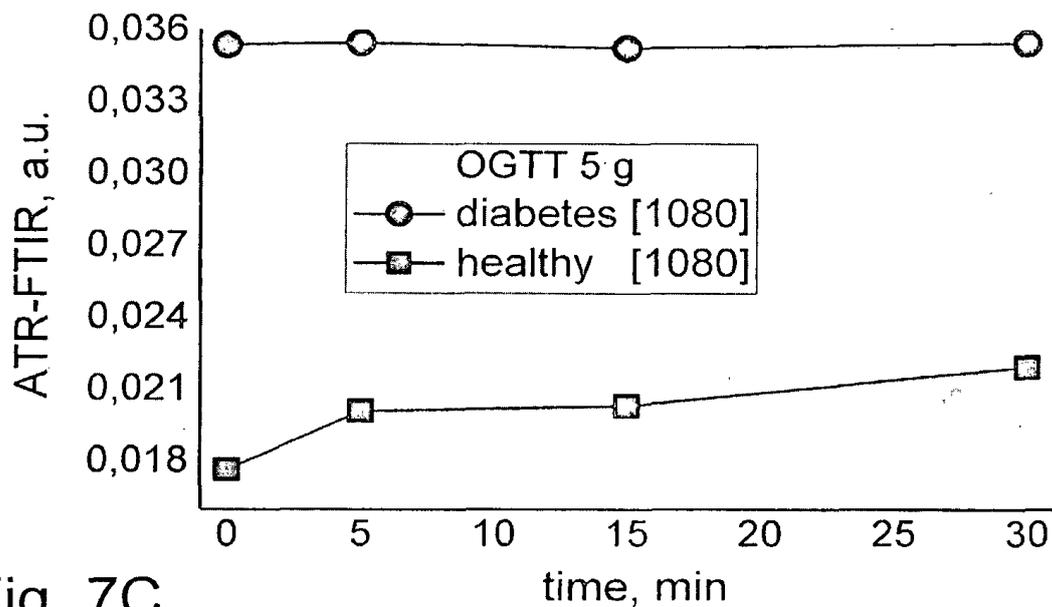
PATENT AGENT [IN/PA-1740]

Fig. 7C

Fig. 8A

Fig. 8B

Fig. 8C

subject 3, OGTT 75 g
— △ — 1030-39
— ▣ — 1080-82
— ○ — 1118-22
— ◇ — 1151-53

Fig. 8D

subject 4, OGTT (75 g)
— △ — 1028-30
— ☐ — 1080
— ○ — 1120-22
— ◇ — 1149-53

Fig. 8E

subject 5, OGTT (75 g)
—△— 1037-1041
—□— 1080-1082
—○— 1120-1122
—◇— 1153

Fig. 8F

—□— healthy (59, M)
—○— DM (S1, 67, M)
—△— DM (S2, 70, F)
—▽— DM (S3, 69, M)
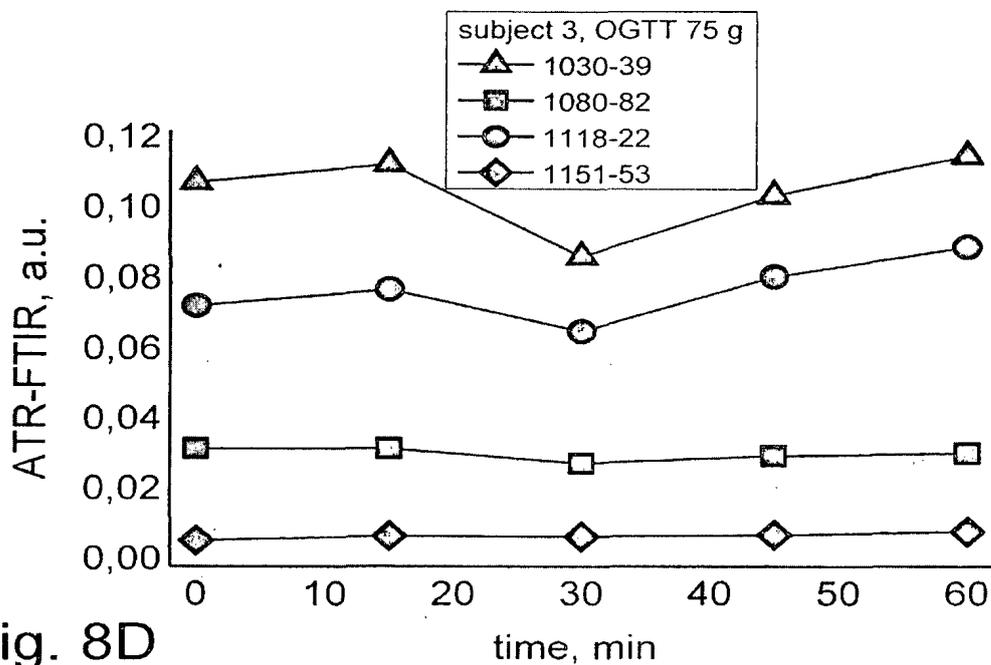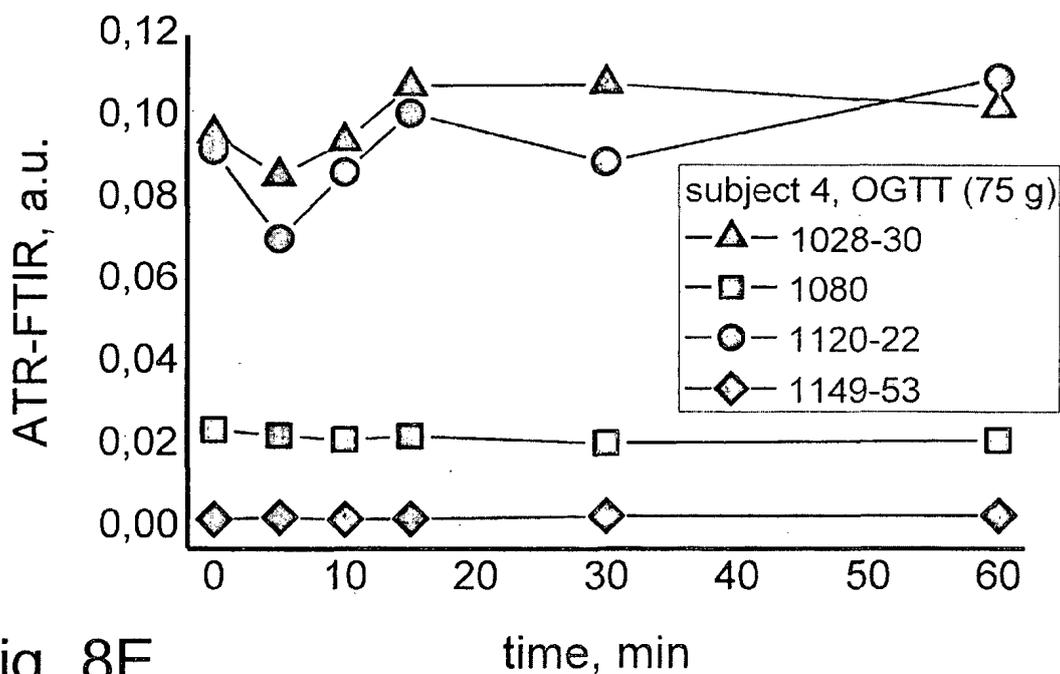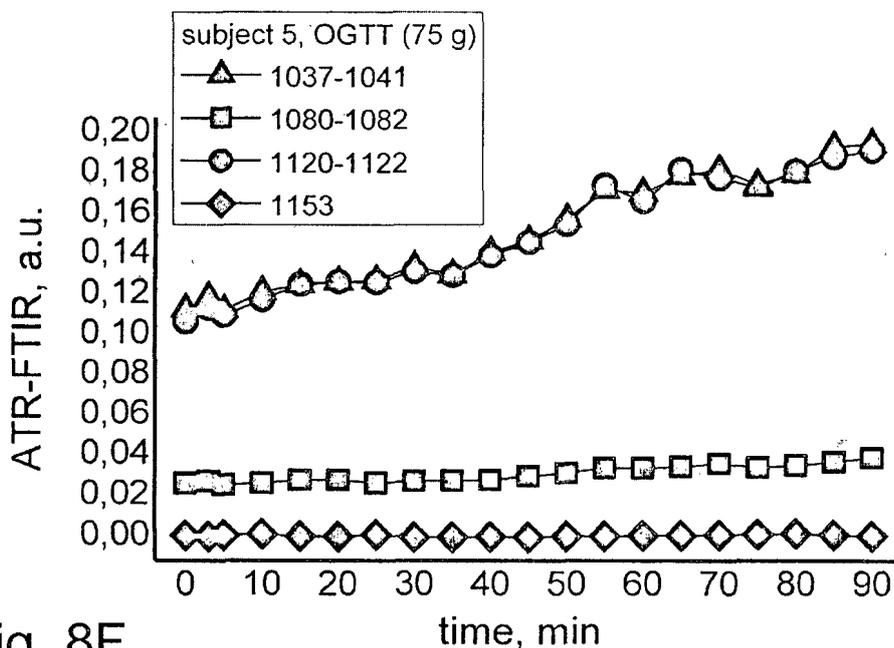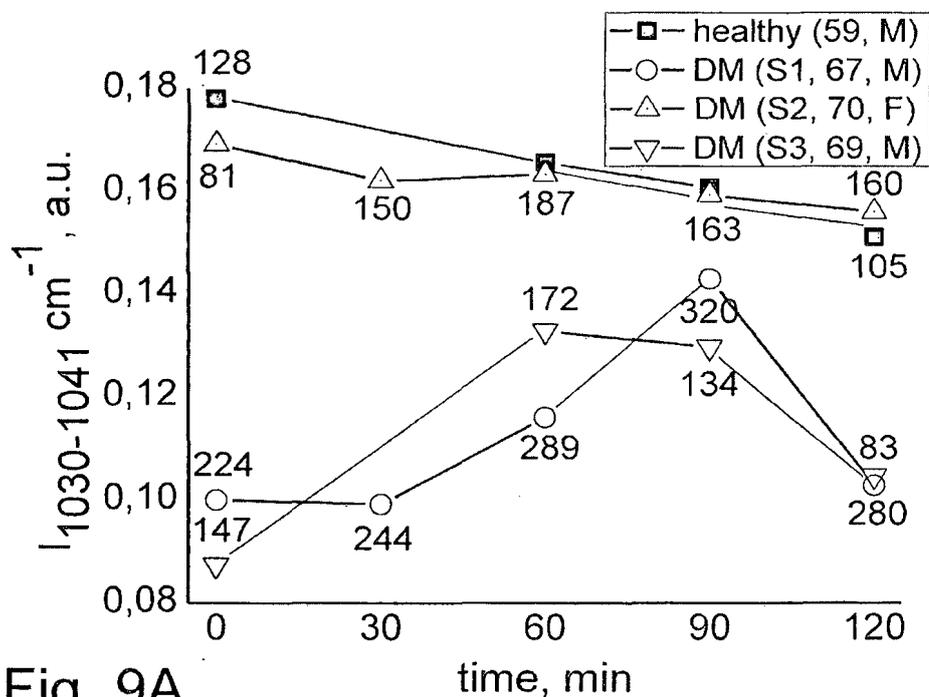
Fig. 9A

(TARUN GANDHI)

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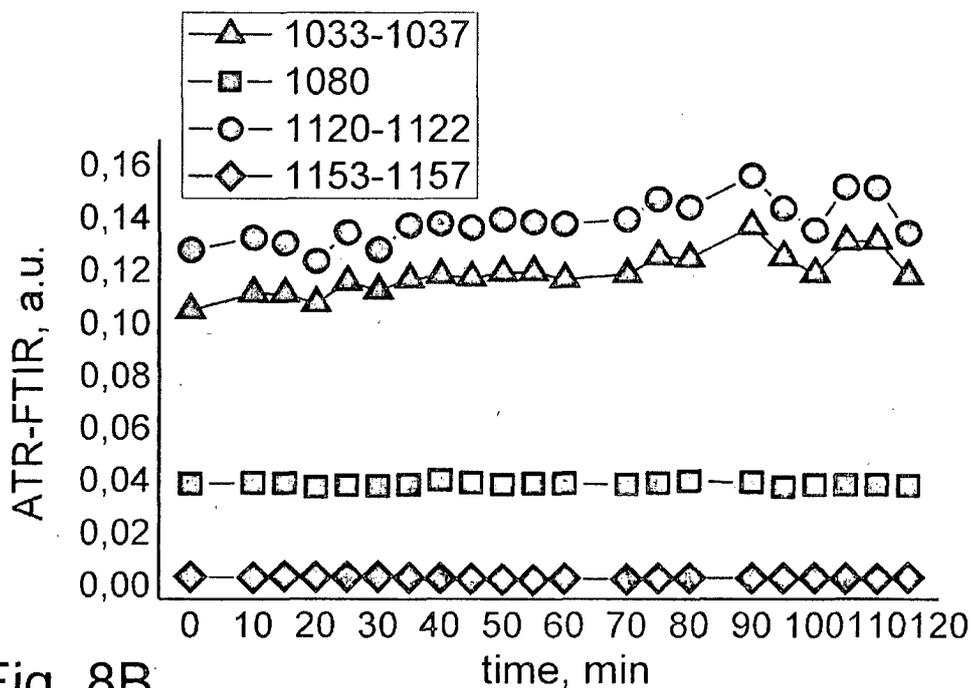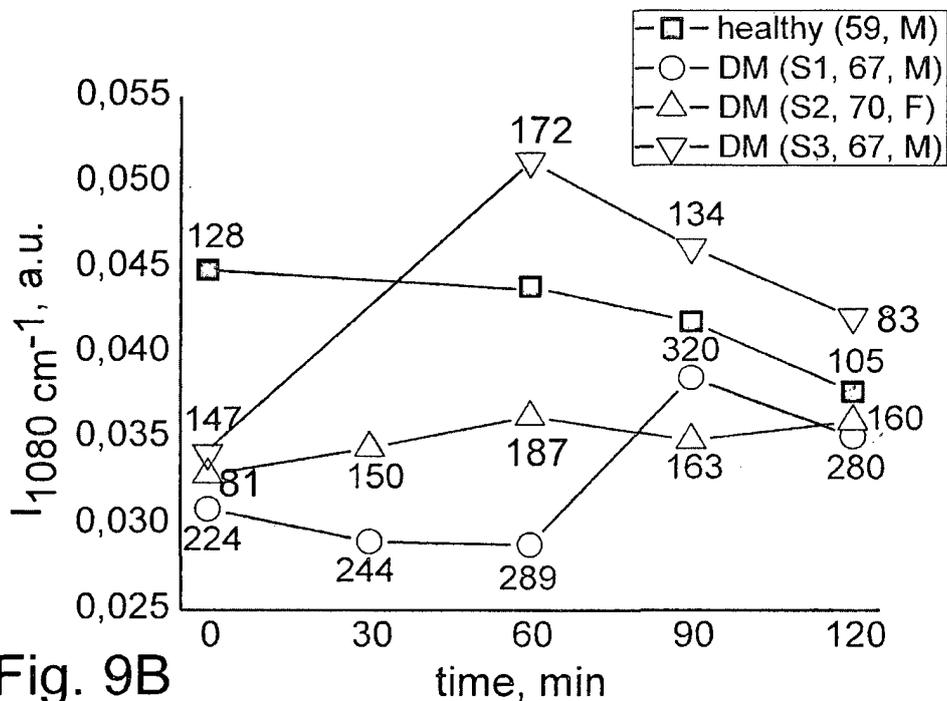
Fig. 9B

Fig. 9C

(TARUN GANDHI)
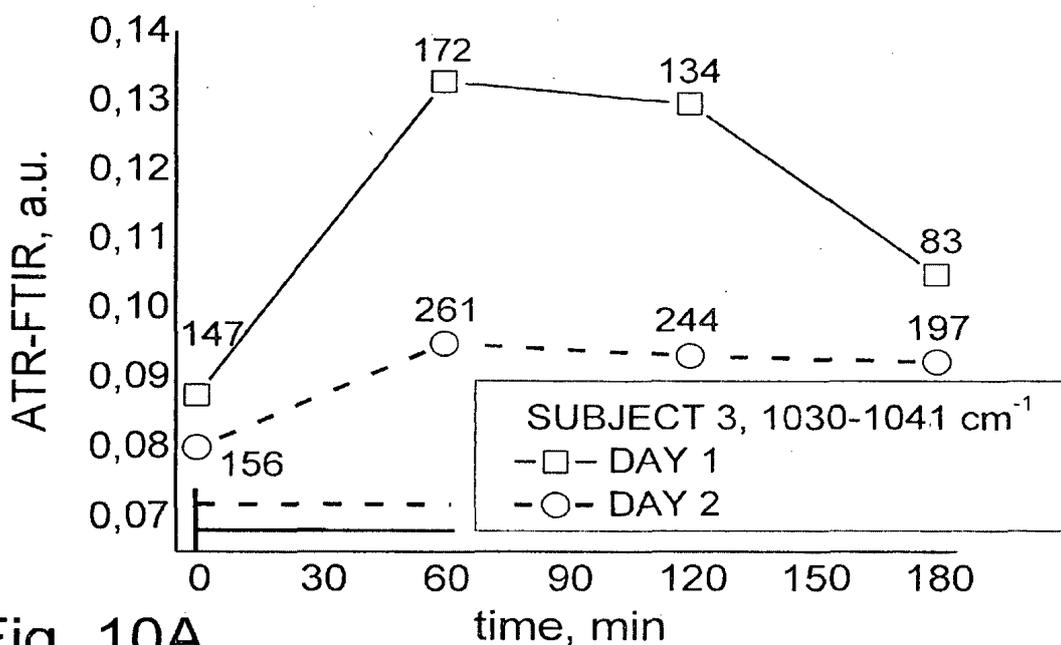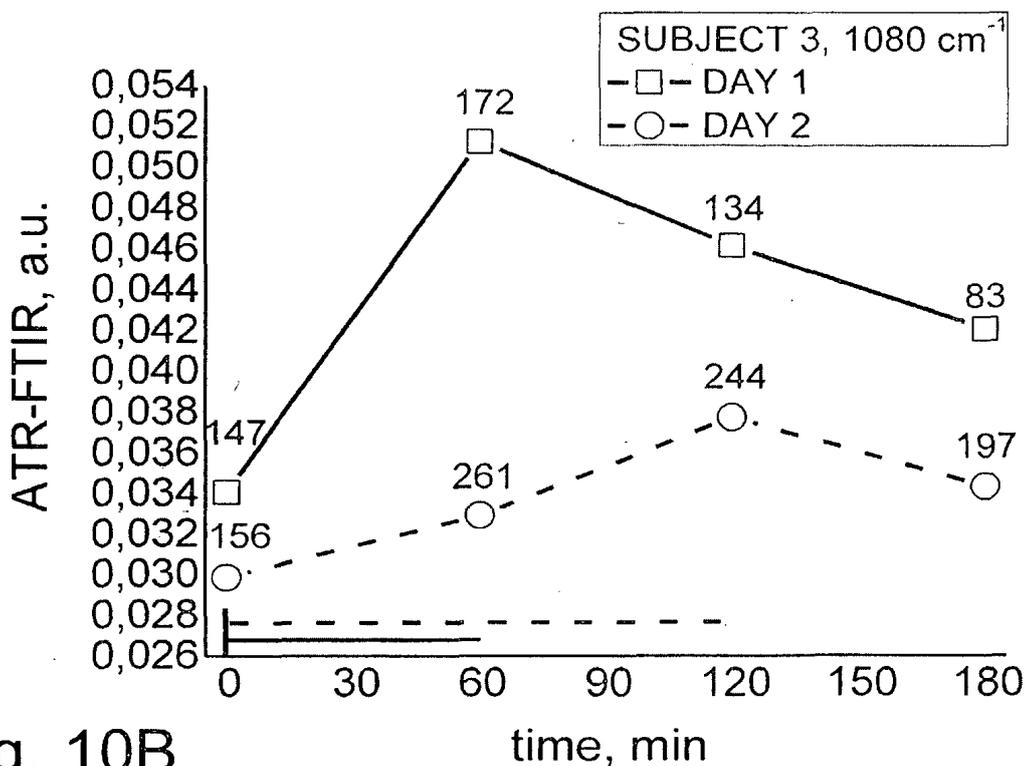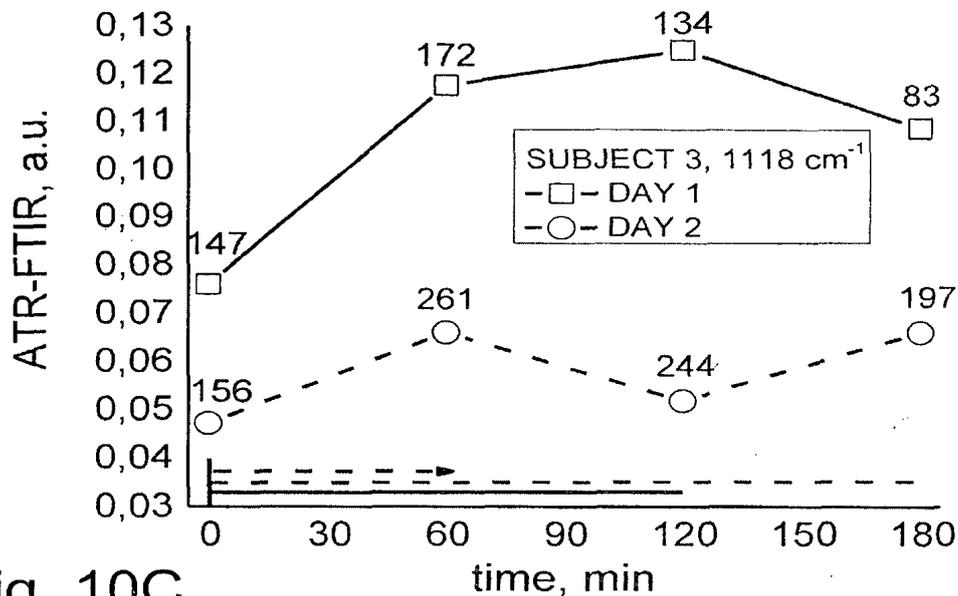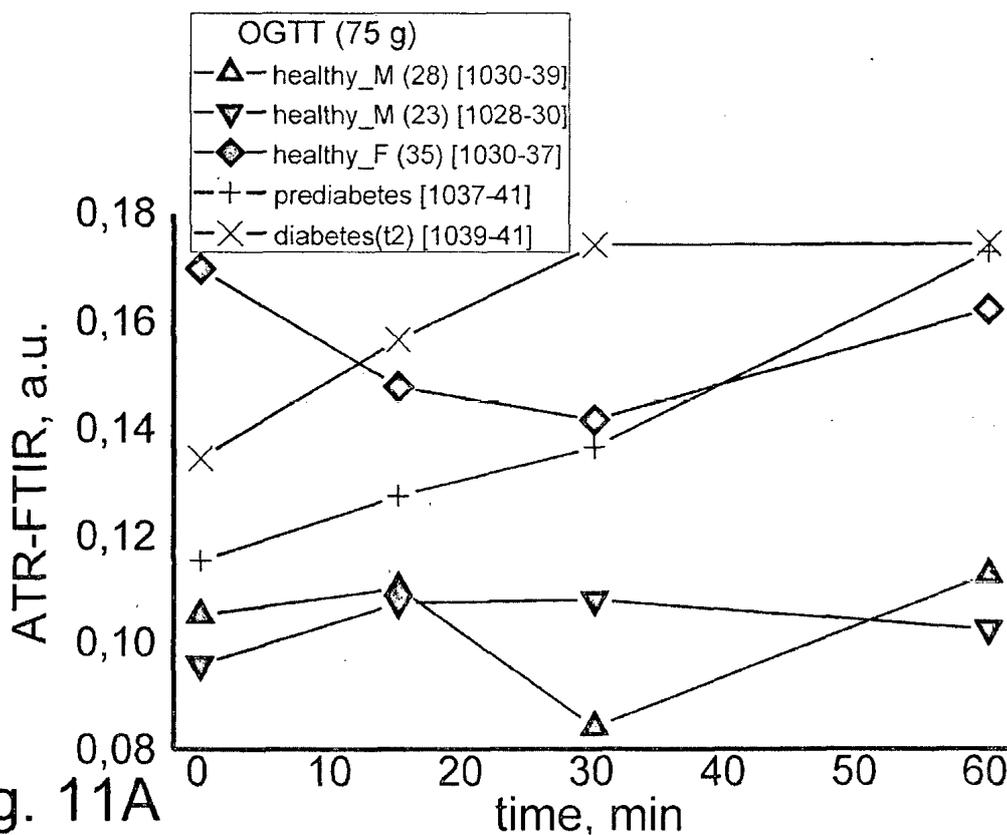
PATENT AGENT [IN/PA-1740]

Fig. 10A

Fig. 10B

Fig. 10C

SUBJECT 3, 1118 cm⁻¹
—□— DAY 1
—○— DAY 2

Fig. 11A

OGTT (75 g)
—△— healthy_M (28) [1030-39]
—▽— healthy_M (23) [1028-30]
—◇— healthy_F (35) [1030-37]
—+— prediabetes [1037-41]
—✕— diabetes(t2) [1039-41]

OGTT (75 g)
- –▲– healthy_M (28) [1080-82]
- –▽– healthy_M (23) [1080]
- –◇– healthy (35) [1080-82]
- –+– preD_pe [1080-82]
- –✕– DM (t2) [1080-82]

Fig. 11B

OGTT (75 g)
- -▲- healthy_M (28) [1120-22]
- -▽- healthy_M (23) [1120-22]
- -◇- healthy_F (35) [1116-18]
- -+- preD [1120-22]
- -✕- DM (t2) [1122]
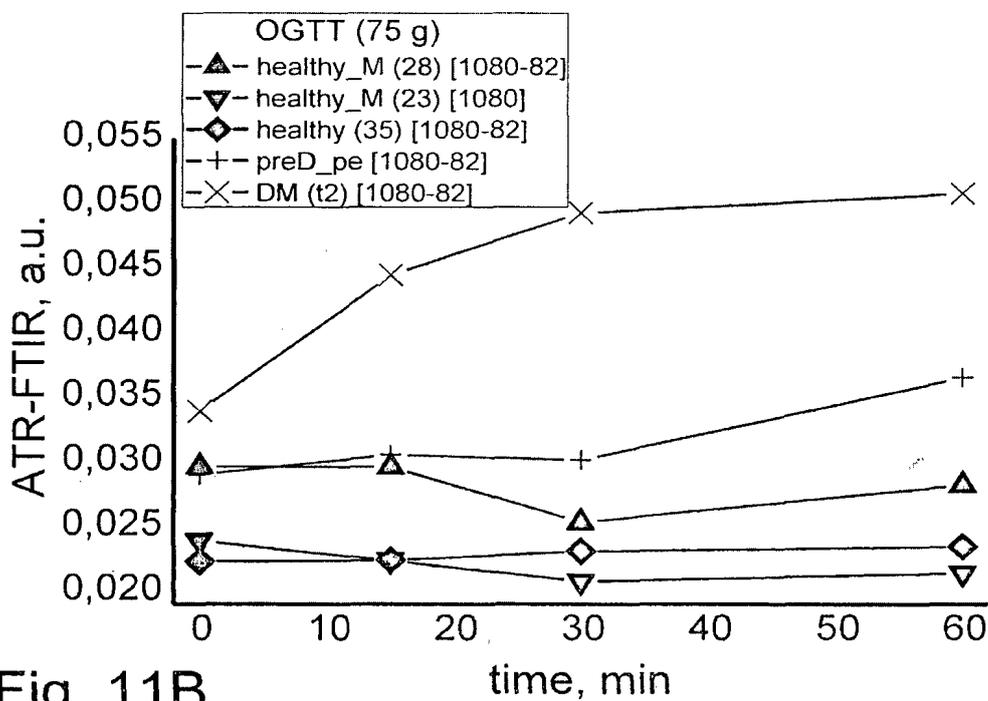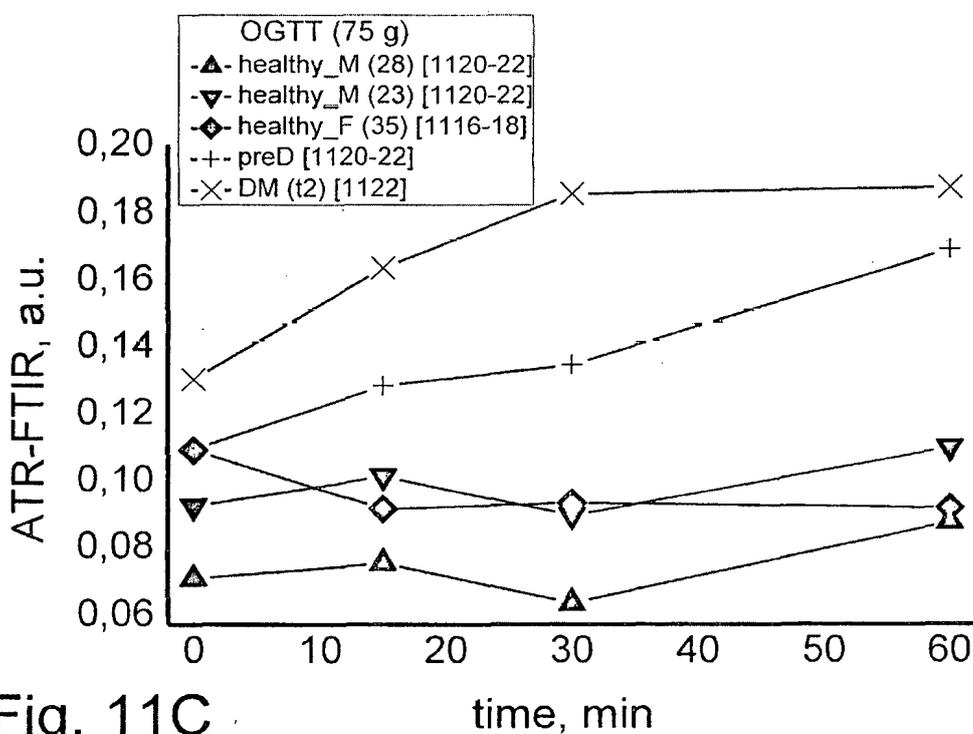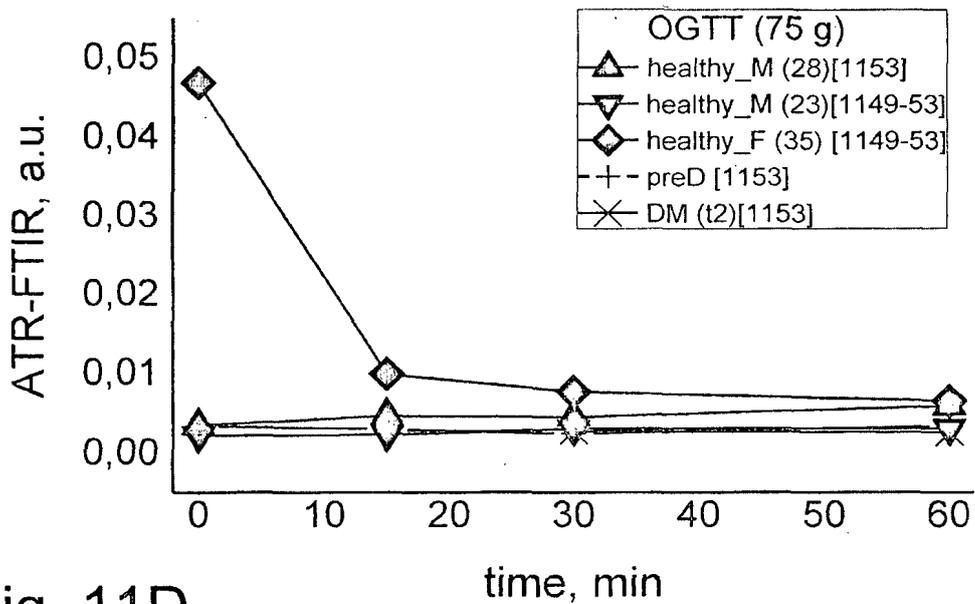
Fig. 11C

(TARUN GANDHI)

PATENT AGENT [IN/PA-1740]

Fig. 11D

1. **TITLE OF THE INVENTION:**

A METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE AND FOR GENERATING PREDICTIVE CLINICAL METRICS

2. **APPLICANT:**

Name: **EIKJE, Natalja**

Nationality: Norway

Address: Urnesveinen 11, Tysvaervaag 5565, Norway.

3. **PREAMBLE TO THE DESCRIPTION:**

The following specification particularly describes the invention and the manner in which it is to be performed:

BACKGROUND OF THE INVENTION
FIELD OF THE INVENTION

The invention relates generally to monitoring metabolic response in a subject, that comprises the step of consecutive performance of a plurality of measurements and further calculations of glucose levels, obtained by HATR-FTIR (horizontally attenuated total reflection Fourier transform infrared) spectroscopy. More particularly, the invention further relates to calculating the LT (lag/latency time) changes between measured in capillary blood the peak glucose level and the peak levels of glucose values by HATR-FTIR spectroscopy after achieved response in test subjects' from the ingestion of quantified amount of pure glucose and post-prandially, allowing to assess stability of metabolic control in healthy, prediabetic and diabetic subjects. Furthermore, qualitative and quantitative interpretation of GV (glycemic variability), calculation of the LT changes, based on a method of simultaneous assessment of 5 glucose-specific values by HATR-FTIR spectroscopy, helps to generate parameters, their characteristics, patterns and, thus, to establish suitable metrics for GV in the clinical practice.

DESCRIPTION OF THE RELATED ART

There are numerous published metrics to quantify different aspects of GV, but still there is no method of GV that is accepted in the clinical practice of diabetes care.

Developing a new set of metrics to evaluate normal, as well as clinically relevant high and low interstitial glucose levels might open for clinicians a new way in the interpretation of the activity of glucose metabolism for diagnosis, treatment and management of the patients with diabetes mellitus and carbohydrate metabolism disorders.

The technique of using ATR-FTIR (attenuated total reflection Fourier transform infrared) spectroscopy has been long known for non-invasive glucose measurement, but through oral mucosa. The drawbacks of such measurements included glucose contamination of the measurement site by food and a highly variable rate of saliva.

Attempts have been made to demonstrate a proof of HATR-FTIR spectroscopy technique to detect, characterize and verify interstitial origin of glucose-specific signals at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} in the skin of healthy, prediabetic and diabetic subjects during OGTT (Oral Glucose Tolerance Test) and post-prandially, randomly and on mornings, i.e. fasting measurements.

Carbohydrate intolerance is one of the major criteria for a diagnosis of diabetes mellitus. OGTT employs ingested carbohydrate in a predetermined form and an amount to quantify a test subject's response to a resulting glucose challenge. However, this test is only concerned with the peak blood level of glucose, but not with the rate of change in glucose levels or the amount of time it takes for glucose levels to fluctuate from a high point to a lower point.

The medical significance of blood glucose fluctuations, i.e. frequency and magnitude, has been a controversial topic and the subject of extensive research, proving that GV can be used to describe a general risk of hyperglycemia over long periods of time, or when focused on events of short duration, such as meals or overnight.

Since glucose on the surface of the skin and within the stratum corneum has been considered as a source for extraneous glucose contamination during testing of invasive glucose monitoring devices, there was not found any direct method for in vivo glucose molecule(s) characterization and monitoring directly on healthy, prediabetes and diabetes subjects.

SUMMARY OF THE INVENTION

An object of the present invention is to provide the user with in vivo method for monitoring individual metabolic response, and for qualitative and quantitative

characterization of GV, in order to further recognize patterns from the patient's data for establishing predictive clinical metrics.

Specifically, the invention is based on calculating the LT changes between the LT measured for the peak of CBG (capillary blood glucose) and the LT for the peaks of epidermally measured interstitial glucose levels by HATR-FTIR spectroscopy on healthy, prediabetic and diabetic subjects under OGTT with different doses (low, medium, high) and post-prandially, applicable for staging Type 2 diabetes and assessing diabetes control, including estimation of intra-day and intra-week risks, as well a general risk of hyperglycemia. More, the invention can be further applied for screening of disorders of glucose metabolism, such as impaired glucose tolerance and diabetes mellitus by means of evaluation of the time required for glucose to diffuse from the capillary to the living skin tissue. In addition, the invention can be also served for individual calibration of obtained glucose profiles by HATR-FTIR spectroscopy in a dynamic time-dependent manner in a subject.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 schematically presents a method for calculation of the LT changes between the LT for the peak of CBG and for the peak of each epidermally measured interstitial glucose level at 1030 cm^{-1}, 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy in a subject.

Figure 2 A-D presents differences between GV obtained between CBG values (shown by dashed lines) and each glucose value (shown by solid lines) at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 1 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Figure 3 A-D presents differences between GV obtained between CBG values (shown

by dashed lines) and each glucose value (shown by solid lines) at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 2 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Figure 4 A-D presents differences between GV obtained between CBG values (shown by dashed lines) and each glucose value (shown by solid lines) at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 3 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Figure 5 A-C presents a comparative dose-dependent GV during monitoring of metabolic response by HATR-FTIR spectroscopy at 1030 - 1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} during OGTT at different doses, at 5 g (low), 20 g (medium) and 75 g (high), in a healthy subject (Subject 4).

Figure 6 A-C presents a comparative dose-dependent GV during monitoring of metabolic response by HATR-FTIR spectroscopy simultaneously shown at 1030 - 1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} during OGTT at different doses, at 5 g (low), 20 g (medium) and 75 g (high), in Subject 3 with Type 2 diabetes.

Figure 7 A-C illustrates examples of characteristic differences in the levels of glucose values and wavenumber shifts at 1118 cm^{-1} (Fig. 7 A-B) and 1080 cm^{-1} (Fig. 7 C) between a healthy subject (Subject 4) and a subject with Type 2 diabetes (Subject 3) under OGTT with different doses at 5 g, 20 g and 75 g of oral glucose.

Figure 8 A-F illustrates a variety of examples of GV simultaneously shown at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy in Type 2 diabetes (Subject 3) under OGTT with 75 g (Fig. 8 A) and 20 g (Fig. 8 B); in a prediabetic subject (Subject 5) under OGTT with 75 g (Fig. 8 F), and in 3 healthy

subjects (Subject 1, Subject 3, Subject 4) under OGTT with 75 g (Fig. 8 C-E).

Figure 9 A-D presents GV simultaneously shown at 1030 - 1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in 3 patients (Subjects 1-3) with Type 2 diabetes, in comparison to a healthy subject (Subject 5).

Figure 10 A-C presents day-to-day variations on GV during a 120-minute post-prandial monitoring of individual metabolic response in Subject 3 with Type 2 diabetes on 2 consecutive days, comparatively shown at 1030 - 1041 cm^{-1}, 1080 cm^{-1} and 1118 cm^{-1} by HATR-FTIR spectroscopy.

Figure 11 A-D comparatively presents GV at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} during monitoring of individual metabolic response in 3 healthy subjects (Subjects 1, 2, 4), in 1 subject as a suspect of having impaired glucose tolerance, i.e. prediabetes (Subject 3), and in 1 subject (Subject 3) with Type 2 diabetes by HATR-FTIR spectroscopy.

BRIEF DESCRIPTION OF THE TABLES

Table 1. LT changes estimated within a 120-minute post-prandial monitoring of metabolic response in 3 subjects with Type 2 diabetes (S1 (Subject 1), S2 (Subject 2) and S3 (Subject 3)) by HATR-FTIR spectroscopy.

Table 2. LT changes between the LT for the peak of CBG and the LT peak for each measured glucose level at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, obtained in a healthy subject during OGTT at different doses (5 g, 20 g, 75 g).

Table 3. LT changes between the LT for the peak of CBG and the LT peak for each measured glucose level at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, obtained in a diabetic subject during OGTT at different doses (5 g, 20 g, 75 g).

Table 4. LT changes at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT with 75 g., i.e. clinical OGTT, in a healthy subject vs. a subject with Type 2 diabetes.

Table 5. LT changes at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} under OGTT with 20 g., i.e. clinical, a healthy subject vs. a subject with Type 2 diabetes.

Table 6. LT changes at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} estimated for the same subject with Type 2 diabetes on 2 consecutive days.

Table 7. OGTT (75 g)., i.e. clinical OGTT, demonstrate estimated LT changes at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} for healthy, prediabetic and diabetic subjects.

DETAILED DESCRIPTION OF THE EMBODIMENT

As described further herein, in vivo glucose spectral measurements from the skin surface of the inner wrists of measured subjects have been performed on a commercially available FT-IR (Fourier transform infrared) spectrometer (Shimadzu IRPrestige - 21/8400S, Japan), that measures the absorbance spectra in the 700-4000 cm^{-1} region at a resolution of 4 cm^{-1}, using 20 frames of accumulation to collect interferogram. Non-invasive glucose monitoring is achieved by tight contact of the measured site with a specially designed flat-plated prism with a mounted ATR crystal for the PIKE Technologies Horizontal accessory (ATR-8200 HA). This horizontal accessory is of a trapezoid shape with carefully chosen dimentions by a manufacturer (80 x 10 x 4 cm), in order to maximize S/N (signal-to-noise) ratio in the measured spectra.

A portable glucosemeter (SKK GluTestS, Sanwa Chemical Institute, Nagoya, Japan) has been used for CBG determinations in mg/dL.

Noninvasive spectroscopic interstitial glucose monitor to an individual necessitates a calibration. Generating such a calibration requires reference CBG values that are uncorrelated to sampling factors. The invented formula provides a method to calibrate dynamic measurements of interstitial glucose values in vivo by HATR-FTIR spectroscopy, based on referenced CBG values, that are described in Figure 1.

A test subject's CBG values are controlled or manipulated through the oral ingestion of

carbohydrate, i.e. meals, and/or through oral consumption of dissolved in water pure glucose at different determined doses (f.e. 5 g, 20 g, 75 g) in such a way that the changes of the targeted glucose profiles of Figures 1-4 are reproduced by the subject's own glucose profiles. Thus, since the subject's CBG is under active control, the influence of other sampling factors are eliminated.

Steps of the invention:
- performing reference CBG measurements at pre-determined intervals prior to spectral acquisition by HATR-FTIR spectroscopy;
- gathering in vivo HATR-FTIR spectra from the forearm of a tested subject at predetermined intervals in the 700-4000 cm^{-1} region with further spectra normalization to amide I, at 1650 cm^{-1}, always after a background scan collection by HATR-FTIR spectroscopy;
- multiple baseline correction of the 1000-1180 cm^{-1} region with assignment of glucose-specific peaks at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, where the bounded peaks at 1030 cm^{-1} and 1041 cm^{-1} are always mentioned together;
- subject's forearm repositioning after each measured spectrum for avoidance of hydration effect;
- manipulating a subject's capillary blood glucose levels in order to obtain meaningful time-dependent LT's and their changes by subject himself/herself under OGTT with different doses (5 g, 20 g, 75 g), post-prandially, or under any other screening metabolic test;
- manipulating a subject's glucose values by HATR-FTIR such those produce meaningful time-dependent changes in the levels of CBG and in the levels of glucose values at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by subject himself/herself under OGTT with different doses (5 g, 20 g, 75 g), post-prandially, or under any other screening metabolic test;
- calculation of the LT changes between the estimated LT for the peak of CBG

and the estimated LT for the peaks of each glucose value at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} measured by HATR-FTIR spectroscopy.

The invention utilizes the targeted glucose profiles by HATR-FTIR spectroscopy schematically presented in Figure 1. "0"- point is pre-prandial, i.e. fasting, and/or before OGTT.

The CBG values and the spectral measurements furnish a data set upon which a calculation of the LT changes is made by using Equation 1, and which a calibration is also based in a subject.

Equation 1 utilizes only parameters described in Figure 1:

LT changes = LT (CBG peak level) − LT (HATR-FTIR peak level(s)$_{(1030/1041/1080/1118/1153\ cm^{-1})}$

The various aspects of the invention are described in greater detail below.

Examples of inducing levels fluctuations/shifts in the subject's CBG values and epidermal glucose values by HATR-FTIR, in order to obtain meaningful time-dependent and dose-dependent glucose values, their LT's for maximum peaks and their LT changes towards monitored characterization of GV in a subject, with or without hyperglycemia, stable or unstable, that can be used to predict the patient's risk of hyperglycemia, to stage Type II diabetes and, in general, to be considered as a new metrics of assessing the quality of metabolic control, are presented in Tables 1-5 and in Figures 2-6.

SUBJECTS

Type 2 diabetes (totally 3 subjects):

Subject 1, Male, age 67, insulin therapy because of recurrent/persistent hyperglycemia, due to no response to orally prescribed tabletes of Metformin for the last 7 years;

Subject 2, Female, age 70, orally prescribed tabletes of Metformin has been changed to a diet control;

Subject 3, Male, age 69, insulin therapy because of recurrent/persistent hyperglycemia, due to no response to orally prescribed tabletes of Metformin for the last 2 years.

Impaired glucose tolerance, i.e. prediabetic subjects, and subjects as suspects of having impaired glucose tolerance due to occasional post-prandial hyperglycemia, based on accepted in the clinical practice interpretation of blood glucose units obtained under different conditions (mg/dL) and according to WHO Diabetes Criteria (totally 3 subjects):

Subject 1, Male, age 49, occasional post-prandial hyperglycemia;

Subject 2, Male, age 58, occasional post-prandial hyperglycemia;

Subject 3, Male, age 49, prediabetes.

Healthy (totally 5 subjects):

Subject 1, Male, age 23;

Subject 2, Male, age 24;

Subject 3, Male, age 60;

Subject 4, Female, age 35;

Subject 5, Male, age 59.

RESULTS

1. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE IN A SUBJECT

(i) individually at each glucose peak value;

(ii) simultaneously at all glucose peak values.

2. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE IN A SUBJECT

(i) in one subject;

(ii) between the subjects.

3. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE IN A SUBJECT

(i) within one group of disease/condition;

(ii) between different groups of diseases/conditions.

4. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE IN A SUBJECT

(i) under one screening test;

(ii) comparatively, under different screening tests.

5. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE IN A SUBJECT

(i) for qualitative interpretation;

(ii) for quantitative interpretation.

6. METHOD FOR MONITORING INDIVIDUAL METABOLIC RESPONSE AND FOR GENERATING PREDICTIVE CLINICAL METRICS IN A PATIENT

(i) for generating a pattern and parameters characterizing GV in the patients with Type

2 diabetes;

(ii) for generating a pattern and parameters characterizing GV in the patients with impaired glucose tolerance, i.e. the patients with prediabetes;

(iii) for generating a pattern and parameters characterizing GV in healthy subjects.

Tables 1-5 describe that:

the LT changes show dose-dependency in healthy, prediabetic and diabetic subjects that differ at duration;

the LT changes are the shortest in a diabetes subject and the longest in a healthy subject, independent of intaken dose of glucose under OGTT;

the LT changes differ at single-, bi-phase- and cascading multi-phase appearance between healthy subjects, subjects as suspects of having impaired glucose tolerance, i.e. prediabetes, and subjects with Type 2 diabetes;

the LT changes show pattern recognition for healthy subjects, prediabetic subjects and subjects with Type 2 diabetes based on the assessed LT changes in minutes;

the LT changes show day-to-day variations, in connection with a pattern recognition.

Figures 2-11, in addition to the results, shown in Tables 1-7, show differences in GV between healthy, prediabetic and diabetic subjects towards their pattern recognition based on specific characteristics:

recognized to healthy and prediabetic/diabetic subjects wavenumber changes, i.e. shifts of glucose-specific peaks to the left or to the right accordingly;

recognized glucose levels as low, medium and high, for healthy, prediabetic and diabetic subjects, assessed at determined time intervals under OGTT with different doses;

recognized meaningful time-dependent fluctuations of GV assessed at each glucose-specific peak value, having common and specific features for healthy, prediabetic and diabetic subjects.

EXAMPLES

EXAMPLE 1

Figure 2 A-D presents differences between GV obtained between CBG values (shown by dashed lines) and each glucose peak value (shown by solid lines) at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 1 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Figure 3 A-D presents differences between GV obtained between CBG values (shown by dashed lines) and each glucose peak value (shown by solid lines) at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 2 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Figure 4 A-D presents differences between GV obtained between CBG values (shown by dashed lines) and each glucose peak value (shown by solid lines) at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in Subject 3 with Type 2 diabetes. The time of increment for each glucose value is indicated by a solid line along x-axis. In case of a biphasic increase, a first phase is indicated by a dashed line along x-axis.

Table 1 displays the LT changes at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} estimated within a 120-minute post-prandial monitoring of metabolic response in 3 subjects with Type 2 diabetes (S1, S2 and S3) by HATR-FTIR spectroscopy.

Subjects	1030-1041 cm^{-1}	1080 cm^{-1}	1118 cm^{-1}	1153 cm^{-1}
S1	0'	0'	0'	30'
S2	0'	0' & 60'	0' & 60'	30'
S3	0'	60'	0'	60'

EXAMPLE 2

Figure 5 A-C presents a comparative dose-dependent GV during monitoring of metabolic response by HATR-FTIR spectroscopy at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} during OGTT at different doses, at 5 g (low), 20 g (medium) and 75 g (high), in a healthy subject (Subject 4).

Table 2 displays the LT changes between the LT for the peak of CBG and the LT peak for each measured glucose peak level at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, obtained in a healthy subject during OGTT at different doses (5 g, 20 g, 75 g).

Healthy	LT	OGTT (5 g)	OGTT (20 g)	OGTT (75 g)
1030-1041 cm^{-1}	LT$_{changes}$	15' & 30'	10'	5' & 30'
1080 cm^{-1}	LT$_{changes}$	15' & 30'	0' & 10' & 20'	5'
1118 cm^{-1}	LT$_{changes}$	10' & 25'	10'	5 '& 25'
1153 cm^{-1}	LT$_{changes}$	35' & 50'	10' & 15'	10'

Figure 6 A-C presents a comparative dose-dependent GV during monitoring of metabolic response by HATR-FTIR spectroscopy simultaneously shown at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} during OGTT at different doses, at 5 g (low), 20 g (medium) and 75 g (high), in Subject 3 with Type 2 diabetes.

Table 3 displays the LT changes between the LT for the peak of CBG and the LT peak for each measured glucose level at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1}, obtained in a diabetic subject during OGTT at different doses (5 g, 20 g, 75 g).

Type 2 diabetes	LT	OGTT (5 g)	OGTT (20 g)	OGTT (75 g)
1030-1041 cm^{-1}	LT$_{changes}$	0' & 10'	0'	0'
1080 cm^{-1}	LT$_{changes}$	10'	15'	0'
1118 cm^{-1}	LT$_{changes}$	0' & 10 & 25'	5'	0'
1153 cm^{-1}	LT$_{changes}$	15' & 25'	25' & 40'	30'

EXAMPLE 3

Figure 7 A-C illustrates examples of characteristic differences in the levels of glucose values and wavenumber shifts between a healthy subject (Subject 4) and a subject with Type 2 diabetes (Subject 3) under OGTT with different doses.

Table 4 displays the LT changes under OGTT with 75 g, i.e. clinical OGTT, a healthy subject vs. a subject with Type 2 diabetes.

Subjects	healthy	Type 2 diabetes
1030-1041 cm^{-1}	15' & 30'	10'
1080 cm^{-1}	15' & 30'	10'
1118 cm^{-1}	10' & 25'	0' & 10' & 25'
1153 cm^{-1}	35' & 50'	15' & 25'

Table 5 displays the LT changes under OGTT with 20 g, a healthy subject vs. a subject

with Type 2 diabetes.

Subjects	healthy	Type 2 diabetes
1030-1041 cm^{-1}	10'	0'
1080 cm^{-1}	0' & 10' & 20'	15'
1118 cm^{-1}	10'	5'
1153 cm^{-1}	10' & 15'	25' & 40'

EXAMPLE 4

Figure 8 A-F illustrates a variety of examples of GV simultaneously shown at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy in Type 2 diabetes (Subject 3) under OGTT with 75 g and 20 g, in a prediabetic subject (Subject 5) under OGTT with 75 g, and under OGTT with 75 g in 3 healthy subjects (Subject 1, Subject 3, Subject 4).

EXAMPLE 5

Figure 9 A-D presents GV simultaneously shown at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy during a 120-minute post-prandial monitoring of individual metabolic response in 3 patients (Subjects 1-3) with Type 2 diabetes, in comparison to a healthy subject (Subject 5). A 120-minute post-prandial monitoring of metabolic response in 3 subjects (S1, S2, and S3) with Type 2 diabetes and 1 healthy control subject ("0"-point is pre-prandial). CBG levels in mg/dL are shown in numbers along curves for each measured subject.

EXAMPLE 6

Fig. 10 A-C presents day-to-day variations on GV during a 120-minute post-prandial monitoring of individual metabolic response in Subject 3 with Type 2 diabetes on 2 consecutive days, comparatively shown at 1030 - 1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} by HATR-FTIR spectroscopy.

Table 6 displays the LT changes estimated for the same subject with Type 2 diabetes on 2 consecutive days.

Subjects	1030-1041 cm^{-1}	1080 cm^{-1}	1118 cm^{-1}	1153 cm^{-1}
S3 (Day 1)	0'	60'	0'	60'
S3 (Day 2)	0'	0'	60'	-

EXAMPLE 7

Figure 11 A-D comparatively presents GV at 1030-1041 cm^{-1}, 1080 cm^{-1}, 1118 cm^{-1} and 1153 cm^{-1} during monitoring of individual metabolic response in 3 healthy subjects (Subjects 1, 2, 4), in 1 subject as a suspect of having impaired glucose tolerance, i.e. prediabetes (Subject 3), and in Subject 3 with Type 2 diabetes by HATR-FTIR spectroscopy under OGTT (75 g).

Table 7 displays OGTT (75 g), i.e. clinical OGTT, demonstrate estimated the LT changes for healthy, prediabetic and diabetic subjects.

Subjects	healthy	prediabetes	Type 2 diabetes
1030-1041 cm^{-1}	5' & 30'	5' & 20' & 30' & 45'	0'

1080 cm^{-1}	5'	5' & 20' & 45'	0'
1118 cm^{-1}	5' & 25'	5' & 20' & 30' & 40'	0'
1153 cm^{-1}	10'	0' & 15' & 25' & 55'	30'