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(54) Title: SAMPLE PREPARATION

(57) Abstract: Methods and apparatus for preparing liquid samples for evaluation are disclosed. The samples are made by dispensing at least one liquid ingredient gravimetrically.



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SAMPLE PREPARATION

This invention relates to the preparation of samples, especially the preparation of multiple samples for use in high throughput testing.

There has been significant interest in recent years in the use of combinatorial chemistry and high throughput testing of materials. Wide varieties of materials, both fluid and solid, have been generated and tested using such techniques. Many of the tests performed have been screening tests, for example a pass/fail test, which do not necessarily require accurate sample formulation. However, in other applications accurate sample formulation be more critical. For example, in determining colour specifications for paints, lacquers, inks etc, the thickness and uniformity of the film may significantly affect the colour determination process.

Colour may be conveniently defined using CIE ($L^*a^*b^*$) 1976 standard (CIELAB) and differences from a defined point in the colour space defined using CIEDE2000 (ΔE_{2000}).

As will be appreciated, paint recipes (or other coloured liquids such as inks) may be defined by measuring the CIELAB values of films formed using the paint (or inks etc) made to a particular recipe and variations from such recipes, for example, owing to changes in ingredients or ingredient sources, may be identified by determining ΔE_{2000} values for films. In determining ΔE_{2000} values for films, a ΔE_{2000} value of around 1 is noticeable to a human observer. Accordingly, ΔE_{2000} values of less than 1, more preferably less than 0.5, are desirable when comparing films with reference CIELAB parameters.

Thus, the accuracy with which such samples are formulated may have a significant effect on whether a particular recipe or colour is acceptable.

Consequently, the potential variability in the amounts of ingredients that are used to make the samples may significantly affect the quality of data generated from the analysis of such samples. For example, the viscosities of liquids vary with fluctuations in ambient temperature. Although the change in viscosity in real terms may be relatively small, it may result in the amount, ie weight, of a sample ingredient used to make the sample being significantly different, for example of the order of 4-5 wt%, and at times up to 15-20 wt%, on a day-to-day basis. Owing to the small size of the samples, such differences in weight deposited may lead to significant differences in the uniformity of samples between batches or day to day basis thus leading to doubts concerning the reproducibility of samples and the data generated therefrom.

It may also lead to time consuming practises such as having to re-calibrate equipment on a relatively frequent basis.

It is an object of the present invention to reduce or obviate the aforementioned disadvantage.

- 5 According to a first aspect of the present invention, a method of sample preparation comprises generating a liquid sample comprising at least two liquid ingredients by dispensing said ingredients to a sample preparation location, gravimetrically controlling the dispensation of at least one of said ingredients and, if necessary, mixing said sample ingredients.
- 10 Preferably, the method comprises volumetrically dispensing a major ingredient of said sample and gravimetrically controlling the dispensation of at least one minor ingredient of said sample. More preferably, said major ingredient comprises at least 50 wt% and up to 99 wt%, more especially at least 70 wt% of a target weight for said sample. Preferably, to achieve the target weight of said sample, said at least one
- 15 minor ingredient is dispensed under gravimetric control in two stages, wherein, in the first stage, a major proportion of said minor ingredient is dispensed at a faster rate than the rate at which a remaining minor proportion of said minor ingredient is dispensed in the second stage.

It will be appreciated that more than one minor ingredient may be added to the major

20 ingredient.

Preferably, in the first gravimetrically-controlled stage of sample generation, between 50 wt% and 98 wt%, more preferably between 50 wt% and 96 wt%, and more especially between 50 wt% and 95 wt% of the ingredient target weight is dispensed. Preferably, in the second gravimetrically-controlled stage of sample generation, up to

25 2 wt%, more preferably up to 4 wt%, and more especially up to 5 wt% of the ingredient target weight is dispensed.

Preferably, the weight of a first ingredient dispensed is measured and used to adjust the weight of a second ingredient dispensed to the sample preparation location wherein the required relative proportions of said ingredients in the sample is

30 achieved.

Using this technique, it has been found that, by using a volumetric dispensation of the major ingredient of the sample, ± 50 mg of a target weight for the major ingredient may be achieved. Using the feedback of the weight of the major ingredient to adjust

the target weight(s) of the or each minor ingredient to maintain proportionality, about $\pm 5\text{mg}$ of a target weight thereof may be achieved.

If the weight of the major ingredient is less than the target weight therefor, the target weight(s) of the or each minor ingredient is adjusted and the or each minor ingredient is added to the major ingredient under gravimetric control. Similarly, If the weight of the major ingredient is more than the target weight therefor, the target weight(s) of the or each minor ingredient is adjusted and the or each minor ingredient is added to the major ingredient under gravimetric control provided that, if the total weight to be dispensed is greater than a predetermined figure, the sample is aborted.

Preferably, during the sample generation, the first volumetric dispensation occurs in not more than 15 seconds/gram (s/g) of sample dispensed, more preferably in not more than 12 s/g, and is typically about 8 s/g. Preferably, the first gravimetrically-controlled stage occurs at a rate of at least 1.5 mg/s, more preferably at a rate of at least 2 mg/s. Preferably, the second gravimetrically-controlled stage occurs at a rate of not more than 1 mg/s, more preferably at a rate of not more than 0.6 mg/s.

In an alternative embodiment, the major ingredient of said sample may also be dispensed under gravimetric control, if desired, also using a two-stage process as described in the preceding paragraphs.

In a yet further alternative embodiment, the major ingredient of said sample may be dispensed in two stages, a first volumetric stage and a second gravimetric stage. The first stage is a volumetric dispensation as described in the preceding paragraphs wherein preferably at least 70% by weight, more preferably at least 80% by weight and, more especially at least 90% by weight, of the major ingredient is dispensed volumetrically. The second stage is a gravimetric stage which may be a single stage or a two-stage process as described in the preceding paragraphs wherein not more than 30% by weight, more preferably not more than 20% by weight and, more especially not more than 10% by weight of the minor ingredient is dispensed gravimetrically.

Some applications may require the preparation of relatively large amounts of samples: such applications may include, for example, identical samples that may be subjected to varying processing conditions such as curing, drying or polymerisation or to varying environmental conditions such as wear testing or weathering of the samples. Preferably, however, in other applications the prepared liquid sample weight is not more than 500g, more preferably not more than 250g. In a particularly preferred embodiment, the prepared liquid sample weight is not more than 100g,

more preferably not more than 10g, and especially not more than 5g. Although target weights of less than 0.1g, may be envisaged in some applications, in applications relating to relatively viscous and/or thixotropic systems, such as paints etc, realistically, the target weight is preferably not less than 0.1g, more particularly not less than 1g.

Samples prepared in accordance with the invention may be used in a variety of high throughput testing techniques.

Usually, an amount of sample greater than that to be dispensed for testing purposes is prepared. Each sample may be prepared individually and/or serially; alternatively, a number of samples may be prepared in parallel.

The sample preparation may include a mixing step if required. The sample may be stirred, shaken, vibrated or otherwise agitated to effect mixing. When the sample is thixotropic in nature, for example paints, effective mixing may be particularly difficult to achieve, especially in small samples. To mix such samples, it is preferred to subject the sample to a three dimensional reciprocating motion such as that imparted by conventional paint can shaker equipment used to mix tinters into base paints to customers' requirements.

The invention also includes apparatus by which the methods of the invention may be performed.

More particularly, according to a second aspect of the invention, apparatus for preparing samples comprises an ingredient dispensing system for dispensing at least two liquid ingredients, said system being operable to control gravimetrically the dispensation of at least one of said ingredients.

The ingredient dispensing system preferably comprises a reservoir for containing a liquid ingredient, a motive means for dispensing, during use, a liquid ingredient from said reservoir, a balance mechanism on which is locatable an ingredient receptacle, a feedback loop connected between said balance mechanism and said motive means and including a computer means for controlling said motive means whereby, in use, said motive means is controlled by said computer means to dispense a target weight of at least one ingredient, the final amount of ingredient dispensed being controlled in response to weight changes detected by the balance mechanism. Preferably, said motive means is controlled by said computer means such that, in use, the rate at which the ingredient is dispensed is controlled.

Preferably, said reservoir comprises a syringe locatable relative to said motive means such that the plunger thereof is movable by said motive means.

Conveniently, the motive means comprises a stepper motor. Other, less preferred, motive means may be for example hydraulically- or gas-operated piston and cylinder mechanisms.

Preferably, said apparatus also comprises a tray mechanism interposable between said reservoir and the balance mechanism whereby, in use, extraneous drips of liquid from said reservoir are prevented from reaching an ingredient receptacle on said balance mechanism.

Preferably, the ingredient dispensing system comprises a second reservoir for containing a liquid ingredient, a second motive means for dispensing, during use, a liquid ingredient from said second reservoir, said computer means, in use, controlling said second motive means to dispense a liquid ingredient volumetrically from said second reservoir and controlling said first motive means to dispense a liquid ingredient gravimetrically from said first reservoir using feedback from said balance mechanism.

Conveniently, the second motive means comprises a peristaltic pump. Other, less preferred, second motive means may be for example an HPLC or a hydraulically- or gas-operated piston and cylinder mechanism.

Preferably, said computer means is programmed to adjust the weight of at least one ingredient dispensed by operation of said first motive means in response to a weight signal receivable from the balance mechanism representing the weight of an first ingredient dispensed by operation of said second motive means wherein the required relative proportions of said ingredients in the sample is achieved.

Preferably, to achieve a target weight of a sample, said computer means is programmed to control said first motive means to dispense at least one ingredient gravimetrically using feedback from said balance mechanism in two stages, wherein, in the first stage, a major proportion of said minor ingredient is dispensed at a faster rate than the rate at which a remaining minor proportion of said minor ingredient is dispensed in the second stage.

Accordingly, it is preferred that said computer is programmed to control said first motive means, in the first gravimetrically-controlled stage, to dispense between 50 wt% and 98 wt%, more preferably between 50 wt% and 96 wt%, and more especially between 50 wt% and 95 wt% of a target weight for an ingredient. Preferably, said

computer is programmed to control said first motive means, in the second gravimetrically-controlled stage, to dispense up to 2 wt%, more preferably up to 4 wt%, and more especially up to 5 wt% of a target weight for an ingredient.

5 Preferably, said computer is programmed to control said second motive means to dispense an ingredient volumetrically in not more than 15 s/g of sample dispensed, more preferably in not more than 12 s/g and is typically about 8 s/g. Preferably, said computer is programmed to control said first motive means to dispense a first portion of a target weight of an ingredient in a first gravimetrically-controlled stage at a rate of at least 1.5 mg/s, more preferably at a rate of at least 2 mg/s. Preferably, said
10 computer is programmed to control said first motive means to dispense a second portion of a target weight of an ingredient in a second gravimetrically-controlled stage at a rate of not more than 1 mg/s, more preferably at a rate of not more than 0.6 mg/s.

15 In an alternative embodiment, said computer is programmed to control said second motive means to dispense a major ingredient under gravimetric control, preferably using a two-stage process as described in the preceding paragraphs.

In a preferred embodiment of the invention, said sample receptacle comprises a well plate containing a plurality of wells each capable of receiving ingredients of samples. Sample ingredients are dispensed, for example as described previously, in the wells
20 and the wells are sealed. The samples in the wells are then subjected to a mixing step.

Alternatively, and especially for larger sample sizes, individual receptacles, eg pots, having a capacity of for example up to 550g may be used. If preferred, such individual receptacles may be supported in racks for parallel or serial processing.

25 Preferably, the well plate is sealed using a heat sealable foil. The sealed well plate may then be subjected to an appropriate motion, as hereinbefore described, to effect mixing of the sample ingredients.

Preferably, the foil used to seal a well plate is penetrable by for example a dispensing tip whereby, in use, quantities of liquid samples in the wells may be aspirated into
30 said dispensing system for dispensing on a surface of a substrate for subsequent testing.

Alternative sealing means for the wells, or for individual pots, may be used. For example, a sealing plate having individual seals for surrounding each well may be clamped to the well plate. In that instance, the sealing plate may be provided with a

plurality of sample ports or other sample access means positioned to permit samples in the wells to be accessed. Individual pots may be fitted with lids, again with sample access means being provided.

A particularly preferred application for the methods and apparatus of the present invention is in the formation and characterisation of films of coating compositions. Such coating compositions particularly include paints, lacquers, varnishes and the like. In this context, the term "paint" is used to mean coatings for painting the interior and exterior surfaces of structures such as buildings, fences and bridges, for both decorative and/or protective purposes. Paints typically comprise a carrier liquid and a film forming binder polymer together with other components such as additives including thickeners and for coloured paints, pigments. The carrier liquid can comprise water, organic solvent or a mixture of water and organic solvent. The binder polymer may be in the form of a dispersion of particles in the carrier liquid, whereby the polymer exists in particulate form or it may be dissolved in the carrier liquid and be a solution.

Accordingly, the present invention may be used to explore new recipes or to reformulate recipes following changes in ingredients or ingredient sources or to check in-store formulation practises easily and rapidly.

The invention will now be illustrated by reference to the accompanying drawings and following examples. In the drawings:

Figure 1 is a schematic plan view of a sample preparation station;

Figure 2 is a schematic side view of apparatus for gravimetrically dispensing sample ingredients; and

The apparatus in accordance with the invention that is described below with reference to the drawings has been particularly designed to prepare paint samples and is described in that context. Although some of the features of the apparatus are particularly adapted to handling paint ingredients and samples, it will be appreciated that the apparatus is generically applicable to other liquid sample systems and is not intended to be limited specifically to paint samples.

A sample preparation station 10 is shown in Figure 1. The station 10 has a base plate 11 on which is mounted an automated XYZ handling system 12, for example a robotic movement arm available from Tecan UK Limited which services two dispense stations 14, 16. The system 12 is provided with two sets of grippers (not shown). The first set of grippers is used to load/unload well plates 18 (see Figure 2) from a

well plate storage unit 20 located between the dispense stations 14, 16 to each of the dispense stations 14, 16. The second set of grippers is used to load/unload syringes 22 (see Figure 2) from a syringe storage unit 24 located between the dispense stations 14, 16 to each of the dispense stations 14, 16. A pneumatically-operated
5 heated foil plate sealer 26, for example a plate sealer model number AB-0384-240 available from Abgene for sealing well plates 18 is provided at one end of the station 10.

The well plate storage unit 20 is designed to accommodate thirty five well plates 18. The well plates 18 are conveniently clear plastic microtitre plates each having twenty
10 four wells 28 available from VWR International. The wells 28 are arranged in a 6x4 array and each well 28 has a capacity of about 3.5g. The well plates 18 are bar coded to enable well plate/sample tracking to be performed.

The syringe storage unit 24 is designed to hold up to one hundred 10ml syringes 22, each containing a liquid paint tinter solution 30 (see Figure 2). The unit 24 is
15 temperature and humidity controlled to prevent the paint tinter solutions from drying out.

Each dispense station 14, 16 (see Figure 2) has a four decimal place rapid response balance 32, for example a Mettler SAG 40 available from Mettler Limited. A well plate holder 34 is provided on the balance 32 for holding a well plate 18 in a fixed
20 location. Each dispense station 14, 16 has an automated XY handling system (not shown) on which is mounted a syringe carrier 36 consisting of a frame 38 on which is mounted a micro-stepping stepper motor 40, for example VEXTA 2-phase, 2 amp stepper motor available from The Oriental Motor Company.

The motor 40 is mounted on the frame 38 for reciprocating movement towards and
25 away from the frame 38. In use, a flange (not shown) on the upper end of the syringe plunger 42 engages a slot in the body of the motor 40 and a flange 46 on the upper end of the syringe body 44 engages the frame whereby movement of the motor 40 towards the frame 38 causes liquid to be dispensed from the syringe 22 and slight movement of the motor 40 away from the frame 38 imposes a slight
30 negative pressure on the liquid in the syringe 22 to prevent the formation of extraneous drops of liquid on the nozzle 48 of the syringe 22. Although shown as separate in Figure 2, the frame 38 also has mounted thereon a drip tray 50 which is pneumatically operable to be interposed between the nozzle 48 and a well plate 18.

Each dispense station 14, 16 is provided with at least one peristaltic pump (not
35 shown), for example a peristaltic pump model number 520S/R available from VWR

International. The peristaltic pumps are connected to a base paint reservoir (not shown) which may be either mounted on the base plate 11 of the station 10 or externally thereof. The peristaltic pump(s) at each dispense station 14, 16 are mounted on the base plate 11 with the or each outlet nozzle (not shown) being
5 mounted on the respective XY handling system.

A bar code reader (not shown) is also provided on the base plate 11 of the station 10.

A computer 52 (see Figure 2) is provided to control operation of the sample preparation station 10. In addition to controlling the XYZ and XY handling systems, the computer system controls the peristaltic pumps and the stepper motors 40 and
10 the drip trays 50 and is provided with a feedback loop 54 from the balance 32. The computer also records the well plate bar codes and maintains a record of the sample recipes located in each well 28 of the well plates 18.

In operation, an operator loads the station 10 with the well plates 18, foil seals, base paint and disposable tinter syringes 22. The computer 52 is programmed with the
15 required sample recipes and operation of the system is initiated. The XYZ handling system 12 loads each balance 32 at the respective dispensing stations 14, 16 with a well plate 18, each well plate 18 being passed by the bar code reader on route to the dispensing station 14, 16.

The computer 52 calculates a dispense volume for each well based on the required
20 base paint ingredient weight for each recipe and controls the XY handling system to move the discharge nozzle of the peristaltic pump over each well 28 in the well plate 18 and operates the peristaltic pump to discharge the calculated amount of base plate ingredient for that well 18. As each well 18 is filled with the base paint ingredient, the final weight of the base paint ingredient in the well is recorded by the
25 computer 52. The computer 52 then calculates, based on the final weight of base paint ingredient in each well 18, the weight(s) of tinter ingredient(s) that has to be added to each well 28 to complete the recipe for each well 28.

The XYZ handling system 12 is then operated to load each dispense station 14, 16 with a syringe 22 containing the required tinter ingredient 30. The XY handling
30 system at each dispense station 14, 16 is then operated to position the syringe 22 over each well in sequence to dispense using the stepper motor 40 the required weight of tinter ingredient 30 in each well 28. At the start of dispensing the tinter ingredient 30 into a well 28, the drip tray 50 is withdrawn from beneath the nozzle 48 of the syringe 22 and at the end of the dispense of the tinter ingredient 30, the drip
35 tray 50 is replaced beneath the nozzle 48 of the syringe 22. Additionally, the

computer 52 controls the stepper motor 40 to dispense the tinter ingredient 30 from the syringe 22 relatively rapidly until a major proportion of the tinter ingredient 30 is dispensed and then to control it to dispense the tinter ingredient 30 relatively slowly until the target weight for the tinter ingredient 30 is achieved. At the end of the discharge, the stepper motor 40 is reversed to impose a slightly negative pressure on the tinter ingredient 30 remaining in the syringe 22 to prevent drips. The final weight of the tinter ingredient 30 dispensed into a well 28 is recorded.

As a syringe 22 is exhausted, the XYZ handling system 12 is operated to remove the exhausted syringe from the relevant dispense station 14, 16, dispose of it and to collect and insert a fresh syringe 22.

It will be appreciated that, depending on the recipes for the paint samples loaded in the computer 52, not every well 28 will necessarily receive an amount of a particular tinter ingredient 30. Similarly, paint recipes may well require the inclusion of say up to five or more tinter ingredients, but more typically two or three tinter ingredients, to achieve a particular colour, for example. In such instances, the computer 52 will operate the apparatus to locate in sequence syringes 22 containing different tinter ingredients 30 for dispensation into at least one of the wells 28.

Once all of the samples in a well plate 18 have been completed, the XYZ handling system 12 is operated to remove the completed well plate 18 from the respective dispense station 14, 16 and move it to the plate sealer 26 at which it is sealed with a foil lid.

Following completion of all of the well plates 18 for a particular set of recipes, the well plates 18 are manually loaded in batches of, for example, ten in a paint shaker device, for example a VIBA 25 available from Collomix, which is then operated to shake the well plates 18 to mix the ingredients of each sample therein.

Once the samples have reached this stage, they may then be tested, for example by being dispensed onto a substrate to form films which are then characterised.

Example 1

Using the apparatus and method described above, water-based latex paint recipes were formulated.

One sample recipe is shown in Table 1 below. The tinters used were made up as 1% weight of pigment in base paint to avoid trying to dispense very small quantities of pigments. In formulating the sample, the actual weights of tinters dispensed was the weights dispensed following adjustment of the target weights by the computer

based on the actual weight of the base paint dispensed and gravimetric control of the weights of tinters being dispensed. As can be seen, good control of the target weights was achieved.

Table 1

Ingredient	Target Weight (mg)	Actual Weight (mg)	Difference between target and actual weights (mg)
Base paint	2786.3	2780.8	-5.5
Tinter 1 (black)	28.7	23.9	-4.8
Tinter 2 (yellow oxide)	74.8	75.3	+0.5
Tinter 3 (oxide red)	11.3	11.1	-0.2

5

Example 2

Using the apparatus and methods described above, solvent-based alkyd resin paint recipes were formulated.

One sample recipe is shown in Table 2 below. The tinter used was made up as 1% weight of pigment in base paint to avoid handling very small quantities of pigment. In formulating the sample, the actual weight of tinter dispensed was the weight dispensed following adjustment of the target weight by the computer based on the actual weight of the base paint dispensed and gravimetric control of the weight of tinter being dispensed. As can be seen, good control of the target weights was achieved.

10

15

Table 2

Ingredient	Target Weight (mg)	Actual Weight (mg)	Difference between target and actual weights (mg)
Base paint	2327.7	2325.0	-2.7
Tinter 4 (phthalo blue)	679.0	679.2	+0.2

Claims

1. A method of sample preparation comprises generating a liquid sample comprising at least two liquid ingredients by dispensing said ingredients to a sample preparation location, gravimetrically controlling the dispensation of at least one of said ingredients and, if necessary, mixing said sample ingredients.
2. A method according to claim 1 wherein a major ingredient of said sample is dispensed volumetrically and gravimetrically controlling the dispensation of at least one minor ingredient of said sample.
3. A method according to claim 1 or claim 2 in which at least one minor ingredient of said sample is dispensed under gravimetric control in two stages, wherein, in the first stage, a major proportion of said minor ingredient is dispensed at a faster rate than the rate at which a remaining minor proportion of said minor ingredient is dispensed in the second stage.
4. A method according to any one of the preceding claims in which the weight of a first ingredient dispensed is measured and used to adjust the weight of a second ingredient dispensed to the sample preparation location wherein the required relative proportions of said ingredients in the sample is achieved.
5. A method according to any one of the preceding claims in which a major ingredient of said sample is dispensed with an accuracy of not less than $\pm 50\text{mg}$ of a target weight for the major ingredient.
6. A method according to any one of the preceding claims in which a minor ingredient of said sample is dispensed with an accuracy of not less than about $\pm 5\text{mg}$ of a target weight for the minor ingredient.
7. Apparatus for preparing samples comprises an ingredient dispensing system for dispensing at least two liquid ingredients, said system being operable to control gravimetrically the dispensation of at least one of said ingredients.
8. Apparatus according to claim 7 wherein ingredient dispensing system preferably comprises a reservoir for containing a liquid ingredient, a motive means for dispensing, during use, a liquid ingredient from said reservoir, a balance mechanism on which is locatable an ingredient receptacle, a feedback loop connected between said balance mechanism and said motive means and including a computer means for controlling said motive means whereby, in use, said motive means is controlled by said computer means to

dispense a target weight of at least one ingredient, the final amount of ingredient dispensed being controlled in response to weight changes detected by the balance mechanism.

- 5 9. Apparatus according to claim 8 wherein said motive means is controlled by said computer means such that, in use, the rate at which the ingredient is dispensed is controlled.
10. Apparatus according to claim 8 or claim 9 wherein said reservoir comprises a syringe locatable relative to said motive means such that the plunger thereof is movable by said motive means.
- 10 11. Apparatus according to any one of claims 8 to 10 further comprising a tray mechanism interposable between said reservoir and the balance mechanism whereby, in use, extraneous drips of liquid from said reservoir are prevented from reaching an ingredient receptacle on said balance mechanism.
- 15 12. Apparatus according to any one of claims 8 to 11 in which the ingredient dispensing system comprises a second reservoir for containing a liquid ingredient, a second motive means for dispensing, during use, a liquid ingredient from said second reservoir, said computer means, in use, controlling said second motive means to dispense a liquid ingredient volumetrically from said second reservoir and controlling said first motive means to dispense a liquid ingredient gravimetrically from said first reservoir using feedback from said balance mechanism.
- 20 13. Apparatus according to claim 12 in which said computer means is programmed to adjust the weight of at least one ingredient dispensed by operation of said first motive means in response to a weight signal receivable from the balance mechanism representing the weight of an first ingredient dispensed by operation of said second motive means wherein the required relative proportions of said ingredients in the sample is achieved.
- 25 14. Apparatus according to any one of claims 8 to 13 in which said computer means is programmed to control said first motive means to dispense at least one ingredient gravimetrically using feedback from said balance mechanism in two stages, wherein, in the first stage, a major proportion of said minor ingredient is dispensed at a faster rate than the rate at which a remaining minor proportion of said minor ingredient is dispensed in the second stage.
- 30

Figure 1

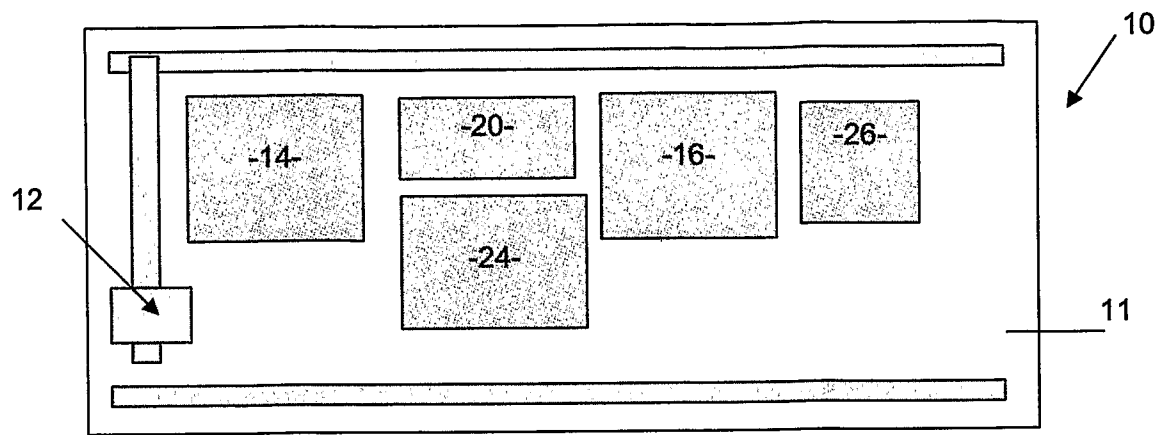
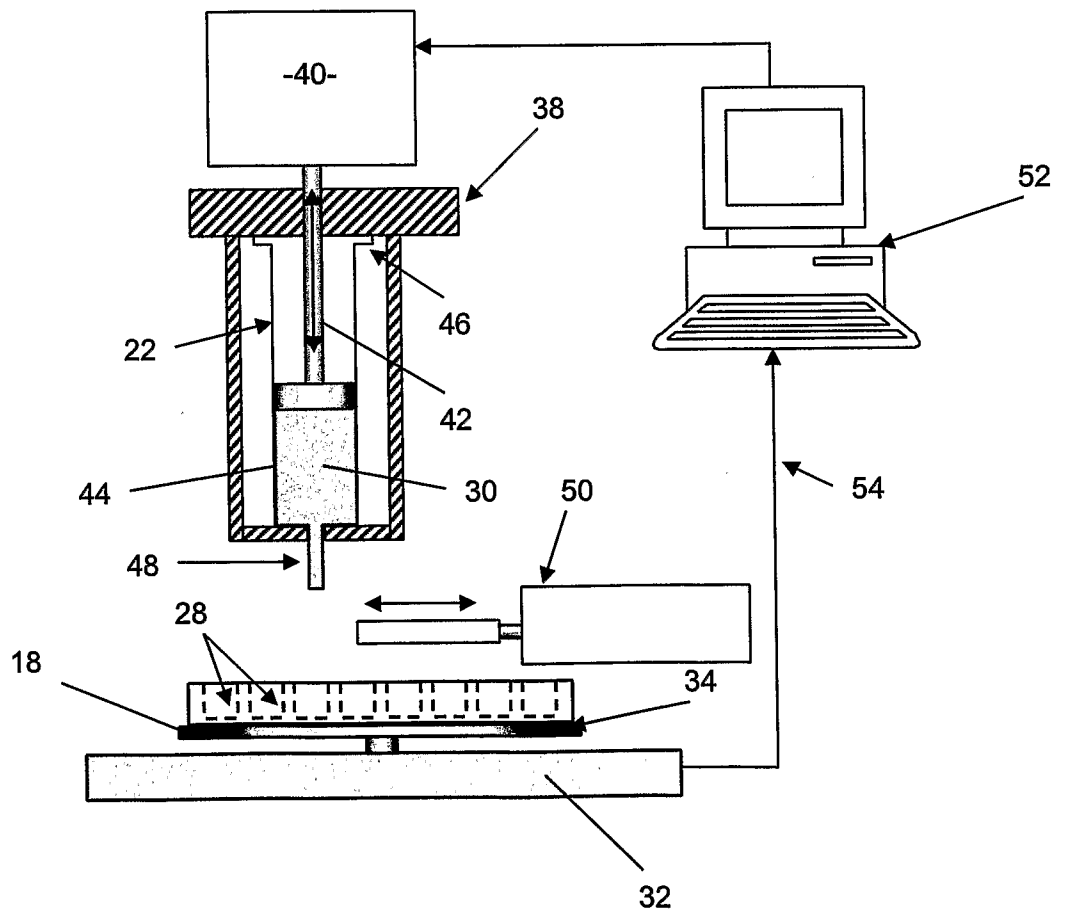


Figure 2



INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2007/001238

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N1/38 G01N35/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N B01F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 350 186 A (SCHALKOWSKY SAMUEL ET AL) 21 September 1982 (1982-09-21) abstract; claims 1-7; figures 1,4 -----	1-14
P, X	US 2006/093515 A1 (FERMIER ADAM M [US] ET AL) 4 May 2006 (2006-05-04) abstract; figures 1,3 paragraph [0022] - paragraph [0038] -----	1-14
X	WO 92/07760 A (DOW CHEMICAL CO [US]) 14 May 1992 (1992-05-14) abstract; figure 1 page 3, line 32 - page 5, line 9 page 6, line 15 - page 8, line 32 ----- -/--	1,2,4,7, 8,10

☒ Further documents are listed in the continuation of Box C.

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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2007/001238

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