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(54) Title: FORMULATION FOR MANUFACTURING A DENTAL COMPOSITE

(57) Abstract: The present invention relates to a formulation comprising a resin phase and an inorganic phase, wherein: - the resin phase comprises a first monomer selected from vinyl monomers comprising at least one hydroxyl or urethane group; a different second monomer selected vinyl monomers with suitable molecular weight, refractive index and viscosity; a different third monomer selected from vinyl monomers with suitable molecular weight, viscosity and log P; a different fourth monomer selected from vinyl monomers comprising at least one polyether group; and a photoinitiator with suitable activity (absorption and/or radical yield) within a 380-450 nm range; and - the inorganic phase comprises micro fillers and nano fillers. The present invention further relates to a manufacturing process of a formulation according to the invention. The present invention further relates to a material resulting from the cure of a formulation according to the invention and to a manufacturing process thereof; and to the use of a formulation or material according to the invention in the manufacture of a dental composite.



FORMULATION FOR MANUFACTURING A DENTAL COMPOSITE

FIELD OF INVENTION

The present invention relates to a composite formulation for use in the manufacture of a
5 composite material by photopolymerization.

The composite formulation or composite material of the invention is useful in the field of dental care and/or in the treatment of a tooth disease such as dental caries.

BACKGROUND OF INVENTION

10 A dental composite formulation is a paste used by dentists for repairing a damaged or unsightly tooth, capable of polymerizing (curing) so as to form a solid material which replaces carried tissues following their removal. Dental composites are currently the primary material for tooth treatment and restoration.

Dental composites formulations typically include a resin phase comprising a mixture of
15 organic monomers and an inorganic phase comprising inorganic fillers. The resin phase generally includes bisphenol A glycerolate dimethacrylate (BisGMA) and/or triethylene glycol dimethacrylate (TegDMA) monomers.

Polymerization is generally initiated by a photoinitiator dispersed in the resin phase of the composite formulation, upon the addition of energy in the form of light irradiation.
20 The dentist applies the composite formulation onto and/or into the damaged tooth and then cures it by using a specific light source ("dental curing light") to supply the light precisely on the composite to be cured.

A typical photoinitiator known in the art is a system consisting of camphorquinone (CPQ) associated with a tertiary amine, which presents an absorption peak at about 460-470 nm.
25 Commercial photoinitiators are generally activated by blue light, i.e. within the 450-495 nm range. The more commonly used curing lights are the Tungsten halogen and light-emitting diode (LED) light sources which emit in the 450-495 nm range.

Dental materials must have good mechanical properties and chemical stability after curing. Indeed, the tooth is submitted to harsh mechanical conditions such as chewing, scraping or tooth brushing. The chemical environment of the mouth is also quite aggressive for the material, e.g. because of saliva acidity. Moreover, dental composites
5 are expected to last for more than a decade.

One important condition for obtaining clinically acceptable properties is that the polymerization reaction should proceed as homogeneously as possible within the formulation, so that the final material is cured homogeneously. Another critical aspect is that the polymerization reaction should be as advanced as possible, so that the final
10 material is cured completely. Inhomogeneous and/or incomplete curing results in the presence of unreacted functions in the dental material, which is thereby less robust and more susceptible to be chemically attacked in the areas comprising unreacted monomers. Polymerization shall also not be limited to the surface of the composite, but must be sufficiently advanced so as to cure the material at clinically acceptable depths which are
15 typically about 2 mm according to the quality standard "ISO 4049" (Third edition, 2000-07-15).

The CPQ/amine photoinitiator system and more generally currently available commercial composite formulations achieve limited polymerization only, i.e. 50-60% within 20 seconds irradiation and at best 60-70% conversion within 40 seconds.

20 Light curing duration is considered as an issue by dental practitioners. Curing time ranges from 20 to 30 seconds for dental composites presently available in the market. This is actually a quite uncomfortable moment for the practitioner who has to remain intensively focussed while holding the dental curing light at arm's length. Failure to maintain focus and/or holding during the cure may result in incomplete and/or inhomogeneous
25 polymerisation, thereby causing a decrease in physical properties and/or chemical stability of the dental material and in the end adverse consequences for the patient.

Safety is another issue related with dental materials. A low degree of cure (incomplete polymerization) can result in free monomers remaining in the material which are susceptible to be released in the mouth and cause local or systemic toxicity, especially

long-term toxicity. In particular the BisGMA and TegDMA monomers typically used in dental compositions are known to negatively impact cellular behaviour, causing inhibition of dentin mineralization processes, genotoxicity and a delayed cell cycle, when released out of the dental material (Krifka, S. *et al.*, *Biomaterials*, March 2013, Vol. 34, pp. 4555-4563.).

Dental composites often include pigments so that the artificial dental material has the same appearance than the natural enamel of the tooth. CPQ/amine system is associated with a yellowing of the dental material due to its absorption peak at 470 nm. Light shades (with low yellowing) of dental composites are therefore difficult to obtain when using CPQ/amine as photoinitiating system. Further, inhomogeneous or incomplete polymerization render the material more permeable (higher water sorption) and thereby causes a slow discoloration of the material. Coloration of a dental material is detrimental to the aesthetic appearance of the treated tooth.

Preliminary research was carried out regarding diphenyl(2,4,6 trimethylbenzoyl)phosphine oxide (TPO) as a substitute photoinitiator system to the CPQ/amine in a model formulation comprising a conventional BisGMA/TegDMA co-monomer resin and an inorganic phase consisting of micro glass and nano silica fillers (Randolph, L. D., PhD thesis, “*Changing CQ for a more efficient photo-initiator in dental filled resins*”, Université catholique de Louvain, September 2017).

Faster polymerization kinetics have been observed in some cases in phosphine oxide-activated composite formulations. However, contrary to conventional photoinitiators, phosphine oxides may be activated at purple light, i.e. 380-450 nm (near-UV) for example in the range 405-410 nm. As the diffraction energy loss increases when the wavelength decreases, in-depth polymerization was difficult to achieve when using phosphine oxides with conventional resins and composites and thus only thin layers (i.e. thickness of about 0.5 mm or less) of pigmented phosphine oxide-activated composite formulations could be manufactured. Therefore, phosphine oxides were not considered as suitable photoinitiators for dental composite formulations.

Therefore, there remains a need for improved compositions for manufacturing dental material, especially compositions with improved mechanical properties, improved chemical stability, reduced curing time, reduced toxicity and/or better aesthetic appearance. It is in fact very difficult to provide substantial innovation in the field of dental composites because, when modifying a composite in order to improve one of its property (e.g. polymerisation yield), this modification most often has a negative impact on others properties (e.g. curing time or aesthetic appearance).

The Applicant carried out in-depth research in order to develop novel composites and designed a formulation based on a resin phase comprising a blend of four different vinyl monomers together with a photoinitiator active at a wavelength ranging from 380 to 450 nm (purple). The Applicant surprisingly found that a formulation according to the invention overcome some of the limitations of prior art dental composites.

SUMMARY

This invention relates to a formulation comprising a resin phase and an inorganic phase, wherein

the resin phase comprises: a first monomer selected from vinyl monomers comprising at least one hydroxyl or urethane group; a different second monomer selected from vinyl monomers having a molecular weight higher than 300 g/mol, a refractive index ranging from 1.5 to 1.7, and a viscosity higher than 1 Pa.s at 25°C; a different third monomer selected from vinyl monomers having a molecular weight lower than 300 g/mol, a viscosity lower than 1 Pa.s at 25°C, and a log P higher than 3; a different fourth monomer selected from vinyl monomers comprising at least one polyether group; a photoinitiator having a molar absorptivity higher than 100 L.mol⁻¹.cm⁻¹ at a spectral wavelength ranging from 380 to 450 nm, a quantum yield of alpha cleavage higher than 0.5 in acetonitrile at a spectral wavelength ranging from 380 to 450 nm, and a solubility higher than 50 g/L in trimethylolpropane triacrylate at 25°C; and, optionally, at least one polymerization inhibitor; and

the inorganic phase comprises micro fillers, preferably mixed oxide glass particles, having a particle size ranging from 1 μm to 10 μm and a refractive index lower than 1.55; nano fillers, preferably amorphous silica, having a particle size ranging from 1 nm to 100 nm; and, optionally, at least one inorganic pigment.

- 5 According to one embodiment, the resin phase is present in an amount ranging from 5% to 60% w/w and the inorganic phase is present in an amount ranging from 40% to 95% w/w, in weight by weight of the total weight of the formulation.

According to one embodiment, the first monomer is selected from acrylates, methacrylates and acrylamides substituted by at least one hydroxyl or urethane group;
 10 preferably the first monomer is selected from diurethane dimethacrylate, 1,3-glyceryl dimethacrylate, polycarbonate dimethacrylate, 3-phenoxy-2-hydroxypropyl-methacrylate, 2-hydroxy-3-phenoxypropyl acrylate, (3-hydroxy-1-adamantyl) 2-methylprop-2-enoate, N,N'-ethylenebis(acrylamide), N,N'-(1,2-dihydroxyethylene)bisacrylamide and pre-reacted oligomers thereof.

- 15 According to one embodiment, the second monomer is selected from acrylates, methacrylates and acrylamides comprising at least one group selected from phenyl, xylyl, naphthyl and combinations thereof; preferably the second monomer is selected from tricyclodecane dimethanol diacrylate, N-benzylmethacrylamide, phenyl methacrylate, benzyl methacrylate, 2,2',6,6'-tetrabromo bisphenol A dimethacrylate, 2-phenoxyethyl
 20 methacrylate, cyclic trimethylol-propane formal acrylate, 2,4,6-tribromophenyl acrylate and ethylene glycol dicyclopentenyl ether acrylate.

- According to one embodiment, the third monomer is selected from acrylates, methacrylates and acrylamides wherein the acrylate, methacrylate and/or acrylamide functions are separated by at least one alkylene backbone; preferably one C₅-C₁₀ alkylene
 25 backbone; preferably the third monomer is selected from 1,6-hexanediol dimethacrylate, 1,6-hexanediol diacrylate, trimethylolpropane trimethacrylate, 1,3-propanediol dimethacrylate, 1,4-butanediol dimethacrylate, 1,10-decanediol dimethacrylate, 1,12-dodecanediol dimethacrylate, pentaerythritol tetramethacrylate, 1,6-hexanediol diacrylate, 1,4-butanediol diacrylate, 1,10-decanediol diacrylate, 1,12-dodecanediol

diacrylate, pentaerythritol tetraacrylate, N,N'-hexamethylenebis(methacrylamide) and trimethylolpropane propoxylate triacrylate.

According to one embodiment, the fourth monomer is selected from acrylates, methacrylates and acrylamides comprising at least one polyether group; preferably the
5 fourth monomer is selected from tetraethylene glycol dimethacrylate, poly(ethylene glycol) methacrylates comprising at least two methacrylate groups and poly(ethylene glycol) diacrylamides; more preferably from poly(ethylene glycol) dimethacrylate and poly(ethylene glycol) diacrylate.

According to one embodiment, the photoinitiator is selected from organophosphine
10 oxides; preferably the photoinitiator is selected from diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide, bis(2,6-dimethoxybenzoyl)-2,4,4-trimethylpentyl phosphine oxide and phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide.

According to one embodiment, the first monomer is present in an amount ranging from 25% to 75% w/w, the second monomer is present in an amount ranging from 1% to
15 50% w/w, the third monomer is present in an amount ranging from 1% to 50% w/w, the fourth monomer is present in an amount ranging from 1% to 25% w/w and the photoinitiator is present in an amount ranging from 0.01% to 2.5% w/w, in weight by total weight of the resin phase.

According to one embodiment, the micro fillers are present in an amount ranging from
20 60% to 99% w/w and said nano fillers are present in an amount ranging from 1% to 40% w/w, in weight by total weight of the inorganic phase.

According to one embodiment, the formulation is free of bisphenol A glycerolate dimethacrylate and/or triethylene glycol dimethacrylate.

This invention also relates to a material resulting from the cure of a formulation according
25 to the invention.

This invention also relates to a process for manufacturing a formulation according to the invention, comprising: (a) Mixing the first, second, third and fourth monomers so as to obtain a resin blend; (b) Adding and dispersing in the resin blend obtained at step (a) the

photoinitiator and optionally at least one polymerization inhibitor as powders, so as to obtain the resin phase of the formulation; and (c) Adding and dispersing in the resin phase obtained at step (b) the nano fillers, then the micro fillers, and then optionally at least one pigment, so as to obtain the formulation.

- 5 This invention also relates to a process for manufacturing a material comprising:
 (A) Providing a formulation according to the invention; (A-1) Optionally, applying said
 formulation into and/or onto a tooth; and (B) Photopolymerizing the formulation by
 applying artificial light at a spectral wavelength ranging from 380 to 450 nm; preferably
 ranging from 400 to 410 nm; preferably wherein said artificial light has an intensity of at
 10 least 1000 mW/cm²; so as to cure the formulation, thereby obtaining the material.

This invention also relates to a formulation according to the invention and/or a material
 according to the invention for use in the treatment of a tooth disease.

This invention also relates to a formulation according to the invention and/or a material
 according to the invention in the manufacture of a dental composite.

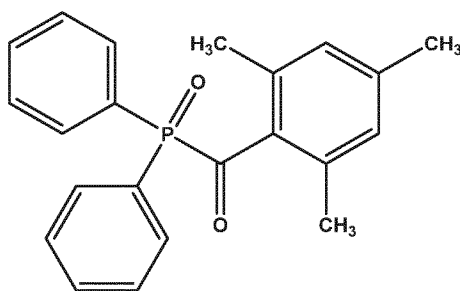
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DEFINITIONS

In the present invention, the following terms have the following meanings:

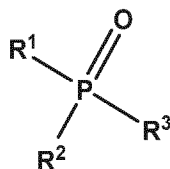
- “**About**” preceding a figure means plus or less 10% of the value of said figure.
- “**Acrylate**” refers to a monomer comprising at least one acrylate group such as for
 20 example monoacrylates, diacrylates or polyacrylates.
- “**Alkyl**” refers to any saturated, linear or branched hydrocarbon chain, preferably
 containing 1 to 12 carbon atoms, and more preferably 1 to 6 carbon atoms, such as
 for example methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl or tert-butyl.
- “**Alkylene**” refers to a saturated, linear or branched divalent alkyl radical such as for
 25 example -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -CH(CH₃)CH₂-, -CH₂CH₂CH₂CH₂-, -CH
 (CH₃)CH₂CH₂-, -CHCH(CH₃)CH₂ or -C(CH₃)₂CH₂-.

- “**Aryl**” refers to a polyunsaturated, aromatic hydrocarbyl group having a single ring or multiple aromatic rings fused together (such as naphthyl) or linked covalently, preferably containing 5 to 20 carbon atoms, and more preferably 6 to 12 carbon atoms, having one or more aromatic rings such as for example phenyl, biphenyl, 1-naphthyl, 2-naphthyl, tetrahydronaphthyl, indanyl or binaphthyl. Preferably, an aryl is not Bisphenol A or one of its derivatives.
- “**Diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide**” or “**TPO**” refers to the compound of CAS number [75980-60-8], of formula:



- “**Log P**” refers to the logarithm of the partition coefficient **P** of a compound. The partition coefficient **P** is the ratio of concentration of said compound in water to the concentration in octanol, as the neutral molecule. **P** and **Log P** can be determined according to procedures known in the art, for example by using a suitable liquid chromatography method (e.g. HPLC) as described for instance in “OECD guideline for testing of chemicals”, P117, March 1989 and in Tolls, J. *et al.*, Environmental Toxicology and Chemistry, May 2003, Vol. 22, No. 5, pp. 1051-1057.
- “**Methacrylate**” refers to a monomer comprising at least one methacrylate group such as for example mono-methacrylates, dimethacrylates or polymethacrylates.
- “**Molar absorptivity**” refers to the absorbance of a compound at a given wavelength, typically when dissolved in a solvent to yield a concentration of 1M solution of analyte in a 1 cm cell or measuring path. The molar absorptivity of a compound can also be described as its molar extinction coefficient, denoted by “ ϵ ”. It can be determined according to procedures known in the art, for example by using a spectroscopic method (e.g. UV-VIS spectrometer with a cuvette analyser) as described for instance in Neumann, M. G. *et al.*, Journal of Dentistry, 2005, Vol. 33, pp. 525-532.

- “**Molecular weight**” refers to the mass of molecule, especially an organic molecule such as a monomer.
- “**Organophosphine oxide**” refers to a compound of general formula:



- 5 wherein **R¹**, **R²** and **R³** are each independently selected from alkyl, aryl, -O-alkyl (alkyloxy), -O-aryl (aryloxy), -C(O)-alkyl and -C(O)-aryl groups; the groups being optionally substituted by at least one alkyl or aryl substituent.

Preferably, **R¹** and **R²** are aryl groups optionally substituted by at least one alkyl substituent, such as for example phenyl, xylyl or naphthyl. Preferably, **R³**
10 is -C(O)-aryl group optionally substituted by at least one alkyl substituent, such as for example benzoyl or trimethylbenzoyl.

- “**Particle size**” refers to the physical dimension of a solid particle. It can be determined according to procedures known in the art, for example by using laser diffraction analysis.
- 15 - “**Quantum yield**” refers to the efficiency of photon absorption and conversion of a photo-initiator, defined as the ratio of the number of photons absorbed to the number of photo-initiator molecules converted to radicals. It can be determined according to procedures known in the art, for example by using a UV-VIS spectrometer as described for instance in Kuhn, H. J. *et al.*, Pure and Applied Chemistry, 2004,
20 Vol. 76, No. 12, pp. 2105-2146. and Chen, Y.-C. *et al.*, Dental Materials, 2007, Vol. 23, pp. 655-665.
- “**Radio-opacity**” refers to the ability to provide opacity to X-rays or other radiation. Radio-opacity may for example be characterized as an opacity equal to or greater than that of the same thickness of aluminium, according to the quality standard “ISO 4049”
25 (*Third edition, 2000-07-15*).
- “**Refractive index**” refers to the dimensionless number of a medium which describes how light propagates through said medium, or how much light is bent when entering

said medium. It can be determined according to procedures known in the art, for example by using a refractometer.

- “**Solubility**” refers to the ability of a solid or liquid substance (called solute) to dissolve in a liquid solvent or substance, especially a liquid monomer. It can be determined according to procedures known in the art, for example by using the well-known “excess solid” or “excess solvent” method.
- “**Viscosity**” refers to the resistance of a fluid to a shearing flow. It can be determined according to procedures known in the art, for example by using a rheometer equipped with a parallel plate geometry of suitable dimensions. More specifically, a rotational rheometer equipped with a temperature controller (cartridge system) and 8 mm plate accessory may be used (Kinexus, Malvern). The bottom plate temperature is controlled to 25 °C (+/- 0.01°C, manufacturer specifications). Ambient light should be filtered between 380-500 nm. To measure the viscosity, about 100 mg of formulation is placed between the plates and the gap is reduced to 1 mm (10 N maximum normal force during descent), or until the paste flows slightly to the side. Any bulging excess is removed. The position is held for 5 seconds. The formulation is then submitted to a frequency sweep (from 0.1 to 100 rad/s, 30 s integration time, 1 mN.m torque). The viscosity at 1 rad/s is calculated from the data by the software installed on the PC controlling the rheometer.

20

DETAILED DESCRIPTION

This invention relates to a **composite formulation** comprising an inorganic phase and a resin phase comprising a mixture of four different monomers and a photoinitiator which is activated by irradiation of purple light, i.e. light having a wavelength ranging from 380 to 450 nm.

25

Each of the four monomers is preferably selected from vinyl monomers.

According to one embodiment, the formulation comprises a resin phase and an inorganic phase, wherein:

the resin phase comprises:

- 5 - a first monomer selected from vinyl monomers comprising at least one hydrogen-donor group;
- a different second monomer selected from vinyl monomers having:
 - a molecular weight higher than 300 g/mol,
 - a refractive index ranging from 1.5 to 1.7, and
 - a viscosity higher than 1 Pa.s at 25°C;
- 10 - a different third monomer selected from vinyl monomers having:
 - a molecular weight lower than 300 g/mol,
 - a viscosity lower than 1 Pa.s at 25°C, and
 - a log P higher than 3;
- a different fourth monomer selected from vinyl monomers comprising at
15 least one hydrogen-acceptor group; and
- a photoinitiator having:
 - a molar absorptivity higher than 100 L.mol⁻¹.cm⁻¹ at a spectral
wavelength ranging from 380 to 450 nm (i.e., the low end of the visible
spectrum, i.e., the “purple” color range),
 - 20 a quantum yield of alpha-cleavage higher than 0.5 in acetonitrile at a
spectral wavelength ranging from 380 to 450 nm, and
 - a solubility higher than 50 g/L in trimethylolpropane triacrylate at 25°C;

and

the inorganic phase comprises micro fillers and nano fillers.

- 25 The resin phase is preferably present in an amount ranging from 1% to 75% w/w, in weight by weight of the total weight of the formulation. According to one embodiment,

the resin phase is present in an amount ranging from 5% to 60% w/w. In one embodiment, the resin phase is present in an amount ranging from 10% to 55% w/w, e.g. ranging from 15% to 25% w/w, ranging from 20% to 30% w/w, ranging from 25% to 35% w/w, ranging from 30% to 40% w/w, ranging from 35% to 45% w/w or ranging from 45% to 50% w/w.

The inorganic phase is preferably present in an amount ranging from 25% to 99% w/w, in weight by weight of the total weight of the formulation. According to one embodiment, the inorganic phase is present in an amount ranging from 40% to 95% w/w. In one embodiment, the inorganic phase is present in an amount ranging from 45% to 90% w/w, e.g. ranging from 50% to 60% w/w, ranging from 55% to 65% w/w, ranging from 60% to 70% w/w, ranging from 65% to 75% w/w, ranging from 70% to 80% w/w or ranging from 75% to 85% w/w.

According to one embodiment, the **first monomer** comprises at least one hydrogen-donor group. In one embodiment, the first monomer comprises at least two hydrogen-donor groups. In one embodiment, the at least one hydrogen-donor group is hydroxyl or urethane group.

According to one embodiment, the first monomer is selected from vinyl monomers. In one embodiment, the first monomer is selected from divinyl monomers.

According to one embodiment, the first monomer is selected from acrylates, methacrylates and acrylamides substituted by at least one hydroxyl or urethane group. According to one embodiment, the first monomer is selected from acrylates and methacrylates substituted by at least one hydroxyl or urethane group. In one embodiment, the at least one hydrogen-donor group is hydroxyl or urethane group. In one embodiment, the first monomer is selected from acrylates and methacrylates substituted by at least one hydroxyl or urethane group.

According to one embodiment, the first monomer is selected from diurethane dimethacrylate (UDMA) [CAS number 72869-86-4], 1,3-glyceryl dimethacrylate, polycarbonate dimethacrylate, 3-phenoxy-2-hydroxypropyl-methacrylate (PHPM) [CAS number 1709-71-3],

2-hydroxy-3-phenoxypropyl acrylate, (3-hydroxy-1-adamantyl) 2-methylprop-2-enoate, N,N'-ethylenebis(acrylamide), N,N'-(1,2-dihydroxyethylene)bisacrylamide and pre-reacted oligomers thereof. According to one embodiment, the first monomer is selected from diurethane dimethacrylate (UDMA) [CAS number 72869-86-4],
5 1,3-glyceryl dimethacrylate, polycarbonate dimethacrylate and pre-reacted oligomers thereof. In one specific embodiment, the first monomer is diurethane dimethacrylate (UDMA). According to one embodiment, the first monomer is selected from 3-phenoxy-2-hydroxypropyl-methacrylate, 2-hydroxy-3-phenoxypropyl acrylate, (3-hydroxy-1-adamantyl) 2-methylprop-2-enoate, N,N'-ethylenebis(acrylamide),
10 N,N'-(1,2-dihydroxyethylene)bisacrylamide and pre-reacted oligomers thereof. In one specific embodiment, the first monomer is 3-phenoxy-2-hydroxypropyl-methacrylate (PHPM).

According to one embodiment, the first monomer has a molecular weight higher than 150 g/mol, e.g. ranging from 150 to 1000 g/mol. In one embodiment, the first monomer
15 has a molecular weight higher than 300 g/mol, e.g. ranging from 300 to 1000 g/mol. According to one embodiment, the first monomer has a dynamic viscosity higher than 1 Pa.s at 25°C, e.g. ranging from 1 to 100 Pa.s at 25°C.

The first monomer is preferably present in an amount ranging from 10% to 95% w/w, in weight by weight of the total weight of resin phase. According to one embodiment, the
20 first monomer is present in an amount ranging from 25% to 75% w/w. In one embodiment, the first monomer is present in an amount ranging from 30% to 70% w/w, e.g. ranging from 35% to 45% w/w, ranging from 40% to 50% w/w, ranging from 45% to 55% w/w, ranging from 50% to 60% w/w, or ranging from 55% to 65% w/w.

According to one embodiment, the **second monomer** is selected from vinyl monomers.
25 In one embodiment, the second monomer is selected from divinyl monomers.

According to one embodiment, the second monomer is selected from vinyl monomers comprising at least one polarizable group, which in the context of the invention refers to a group which exhibits high molar refraction, i.e. a molecular group with a tendency for charge distribution. In one embodiment, the at least one polarizable group is selected from

aryl groups such as for example phenyl, xylyl or naphthyl, or combinations thereof; groups with carbon-bromine bonds such as for example bromobutyl, bromophenyl, or combinations thereof; or groups with carbon-sulfur bonds such as for example thioether, sulfone, cyclic thiophene, thiadiazole, thianthrene, or combinations thereof. In one
5 specific embodiment, the at least one polarizable group is selected from phenyl, xylyl, naphthyl, and combinations thereof. In one embodiment, the second monomer does not comprise bisphenol A (BPA), bisphenol B (BPB) or bisphenol S (BPS).

According to one embodiment, the second monomer is selected from acrylates, methacrylates and acrylamides. According to one embodiment, the second monomer is
10 selected from acrylates and methacrylates. According to one embodiment, the second monomer is selected from acrylamides.

According to one embodiment, the second monomer is selected from tricyclodecane dimethanol diacrylate (TCCDA) [CAS number 42594-17-2], N-benzylmethacrylamide (N-BMA) [CAS number 3219-55-4] phenyl methacrylate, benzyl methacrylate, 2,2',6,6'-
15 tetrabromo bisphenol A dimethacrylate, 2-phenoxyethyl methacrylate, cyclic trimethylol-propane formal acrylate, 2,4,6-tribromophenyl acrylate and ethylene glycol dicyclopentenyl ether acrylate (EGDCPEA) [CAS number 65983-31-5]. According to one embodiment, the second monomer is selected from tricyclodecane dimethanol diacrylate (TCCDA) [CAS number 42594-17-2], N-benzylmethacrylamide (N-BMA)
20 [CAS number 3219-55-4] phenyl methacrylate, benzyl methacrylate, 2,2',6,6'-tetrabromo bisphenol A dimethacrylate, 2-phenoxyethyl methacrylate, cyclic trimethylol-propane formal acrylate, 2,4,6-tribromophenyl acrylate. In one embodiment, the second monomer is tricyclodecane dimethanol diacrylate (TCCDA). In one embodiment, the second monomer is N-benzylmethacrylamide (N-BMA). In one embodiment, the second
25 monomer is ethylene glycol dicyclopentenyl ether acrylate (EGDCPEA).

According to one embodiment, the second monomer has a molecular weight higher than 300 g/mol, e.g. ranging from 300 to 1000 g/mol.

According to one embodiment, the second monomer has a refractive index ranging from 1.5 to 1.7. In one embodiment, the refractive index ranges from 1.5 to 1.55.

According to one embodiment, the second monomer has a viscosity higher than 1 Pa.s at 25°C, e.g. ranging from 1 to 100 Pa.s at 25°C.

The second monomer is preferably present in an amount ranging from 1% to 75% w/w, in weight by weight of the total weight of resin phase. According to one embodiment, the
5 second monomer is present in an amount ranging from 1% to 50% w/w. In one embodiment, the second monomer is present in an amount ranging from 5% to 45% w/w, e.g. ranging from 10% to 20% w/w, ranging from 15% to 25% w/w, ranging from 20% to 30% w/w, ranging from 30% to 35% w/w, or ranging from 35% to 40% w/w.

According to one embodiment, the **third monomer** is selected from vinyl monomers. In
10 one embodiment, the third monomer is selected from divinyl monomers.

According to one embodiment, the vinyl functions in the third monomer are separated by at least one saturated backbone. In one embodiment, the vinyl functions are separated by at least one alkylene backbone, e.g. one C₅-C₁₀ alkylene backbone.

According to one embodiment, the third monomer is selected from acrylates and
15 methacrylates.

In one embodiment, the third monomer is selected from acrylates, methacrylates and acrylamides wherein the acrylate, methacrylate and/or acrylamide functions are separated by at least one alkylene backbone, e.g. one C₅-C₁₀ alkylene backbone. In one
20 embodiment, the third monomer is selected from acrylates and methacrylates wherein the acrylate and/or methacrylate functions are separated by at least one alkylene backbone, e.g. one C₅-C₁₀ alkylene backbone. In one embodiment, the third monomer is selected from acrylamides wherein the acrylamide functions are separated by at least one alkylene backbone, e.g. one C₅-C₁₀ alkylene backbone.

According to one embodiment, the third monomer is selected from 1,6-hexanediol
25 dimethacrylate (HDDMA) [CAS number 6606-59-3], trimethylolpropane trimethacrylate (TMPTMA) [CAS number 15625-89-5], 1,3-propanediol dimethacrylate, 1,4-butanediol dimethacrylate, 1,10-decanediol dimethacrylate, 1,12-dodecanediol dimethacrylate, pentaerythritol tetramethacrylate, 1,6-hexanediol diacrylate (HDDA) [CAS number

- 13048-33-4], 1,4-butanediol diacrylate, 1,10-decanediol diacrylate, 1,12-dodecanediol diacrylate, pentaerythritol tetraacrylate, N,N'-hexamethylenebis(methacrylamide) and trimethylolpropane propoxylate triacrylate. According to one embodiment, the third monomer is selected from 1,6-hexanediol dimethacrylate (HDDMA) [CAS number 6606-59-3], trimethylolpropane trimethacrylate (TMPTMA) [CAS number 15625-89-5], 1,3-propanediol dimethacrylate, 1,4-butanediol dimethacrylate, 1,10-decanediol dimethacrylate, 1,12-dodecanediol dimethacrylate and pentaerythritol tetramethacrylate. In one embodiment, the third monomer is 1,6-hexanediol dimethacrylate (HDDMA). In one embodiment, the third monomer is trimethylolpropane trimethacrylate (TMPTMA).
- 10 According to one embodiment, the third monomer is selected from 1,6-hexanediol diacrylate (HDDA) [CAS number 13048-33-4], 1,4-butanediol diacrylate, 1,10-decanediol diacrylate, 1,12-dodecanediol diacrylate, pentaerythritol tetraacrylate, N,N'-hexamethylenebis(methacrylamide) and trimethylolpropane propoxylate triacrylate. In one embodiment, the third monomer is 1,6-hexanediol diacrylate (HDDA).
- 15 According to one embodiment, the third monomer has a molecular weight lower than 300 g/mol, e.g. ranging from 200 to 300 g/mol.

According to one embodiment, the third monomer has a viscosity lower than 1 Pa.s at 25°C, e.g. ranging from 0.01 to 1 Pa.s at 25°C.

- 20 According to one embodiment, the third monomer has a log P higher than 3, e.g. ranging from 3 to 10.

According to one embodiment, the third monomer has a volatility lower than 1 Pa at 25°C, e.g. ranging from 0.01 to 1 Pa at 25°C.

- 25 The third monomer is preferably present in an amount ranging from 1% to 75% w/w, in weight by weight of the total weight of resin phase. According to one embodiment, the third monomer is present in an amount ranging from 1% to 50% w/w, in weight by total weight of the resin phase. In one embodiment, the third monomer is present in an amount ranging from 5% to 45% w/w, e.g. ranging from 10% to 20% w/w, ranging from 15% to 25% w/w, ranging from 20% to 30% w/w, ranging from 30% to 35% w/w, or ranging from 35% to 40% w/w.

According to one embodiment, the **fourth monomer** comprises at least one hydrogen-acceptor group. In one embodiment, the at least one hydrogen-acceptor group is a polyether group.

According to one embodiment, the fourth monomer is selected from vinyl monomers. In
5 one embodiment, the fourth monomer is selected from divinyl monomers.

According to one embodiment, the fourth monomer is selected from acrylates, methacrylates and acrylamides. According to one embodiment, the fourth monomer is selected from acrylates and methacrylates. According to one embodiment, the fourth monomer is selected from acrylamides.

10 According to one embodiment, the fourth monomer comprises at least one polyether group.

According to one embodiment, the fourth monomer is selected from tetraethylene glycol dimethacrylate and poly(ethylene glycol) methacrylates comprising at least two methacrylate groups and poly(ethylene glycol) diacrylamides. According to one
15 embodiment, the fourth monomer is selected from tetraethylene glycol dimethacrylate and poly(ethylene glycol) methacrylates comprising at least two methacrylate groups. According to one embodiment, the fourth monomer is selected from poly(ethylene glycol) diacrylamides. In one embodiment, the polyethylene glycol (PEG) backbone consists in 10 to 20 PEG units, preferably 15 PEG units.

20 According to one embodiment, the fourth monomer is selected from poly(ethylene glycol) dimethacrylate (PegDMA) [CAS number 25852-47-5] and poly(ethylene glycol) diacrylate (PegDA) [CAS number 26570-48-9]. In one embodiment, the fourth monomer is poly(ethylene glycol) dimethacrylate (PegDMA) [CAS number 25852-47-5]. In one specific embodiment, the fourth monomer is
25 poly(ethylene glycol) dimethacrylate, Mn 750 (PegDMA, Mn 750). In one embodiment, the fourth monomer is poly(ethylene glycol) diacrylate (PegDA). In one further embodiment, the fourth monomer is poly(ethylene glycol) diacrylate, Mn 575 (PegDA, Mn 575).

The fourth monomer is preferably present in an amount ranging from 0.1% to 50% w/w, in weight by weight of the total weight of resin phase. According to one embodiment, the fourth monomer is present in an amount ranging from 1% to 25% w/w. In one embodiment, the fourth monomer is present in an amount ranging from 1% to 20% w/w, e.g. ranging from 2.5% to 7.5% w/w, ranging from 5% to 10% w/w, ranging from 7.5% to 12.5% w/w, ranging from 10% to 15% w/w, or ranging from 12.5% to 17.5% w/w.

According to one embodiment, the fourth monomer has a molecular weight ranging from 700 to 1000 g/mol.

According to one embodiment, the **photoinitiator** is selected from organophosphine oxides. In one embodiment, the organophosphine oxide comprises at least one electron withdrawing group bound to the phosphorus atom, e.g. aryl groups. In one embodiment, the organophosphine oxide comprises at least one phenyl group. In one specific embodiment, the organophosphine oxide comprises at least two phenyl groups.

According to one embodiment, the photoinitiator is selected from diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (TPO) [CAS number 75980-60-8], bis(2,6-dimethoxybenzoyl)-2,4,4-trimethylpentyl phosphine oxide [CAS number 145052-34-2] and phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide [CAS number 162881-26-7]. In one embodiment, the photoinitiator is diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (TPO). In one embodiment, the photoinitiator is bis(2,6-dimethoxybenzoyl)-2,4,4-trimethylpentyl phosphine oxide. In one embodiment, the photoinitiator is phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide (sometimes referred to as "BAPO" corresponding to "Bi Acyl Phosphine Oxide").

According to one embodiment, the photoinitiator absorbs at the low end of the visible spectrum. This may for example be characterized by a molar absorptivity higher than 100 L.mol⁻¹.cm⁻¹, e.g. ranging from 100 to 500 L.mol⁻¹.cm⁻¹, at a spectral wavelength ranging from 380 to 450 nm. In one embodiment, the spectral wavelength ranges from 400 to 410 nm.

According to one embodiment, the photoinitiator has a quantum yield of alpha cleavage higher than 0.2, e.g. ranging from 0.2 to 0.8, in acetonitrile at a spectral wavelength

ranging from 380 to 450 nm. In one embodiment, the spectral wavelength ranges from 400 to 410 nm.

In the invention, the photoinitiator has a solubility higher than 50 g/L in trimethylolpropane triacrylate at 25°C. According to one embodiment, the photoinitiator
5 has a solubility higher than 100 g/L in trimethylolpropane triacrylate at 25°C, e.g. ranging from 100 g/L to 200 g/L at 25°C. According to one embodiment, the photoinitiator has a solubility higher than 200 g/L in 1,6-hexanediol diacrylate at 25°C, e.g. ranging from 200 g/L to 500 g/L at 25°C.

According to one embodiment, the photoinitiator has a low colour. A low colour may for
10 example be characterized by b*(yellow) parameter lower than 10 in CIE L*a*b* space under D65 illuminant, e.g. b*(yellow) parameter ranging from 1 to 10.

According to one embodiment, the photoinitiator has a volatility lower than 1 Pa at 25°C, e.g. ranging from 0.01 to 1 Pa at 25°C.

The photoinitiator is preferably present in an amount ranging from 0.001% to 10% w/w,
15 in weight by weight of the total weight of resin phase. According to one embodiment, the photoinitiator is present in an amount ranging from 0.01% to 2.5% w/w. In one embodiment, the photoinitiator is present in an amount ranging from 0.05% to 1.5% w/w, e.g. ranging from 0.1% to 0.5% w/w, ranging from 0.25% to 0.5% w/w, ranging from 0.5% to 0.75% w/w, ranging from 0.75% to 1.0% w/w, or ranging from 1% to
20 1.25% w/w.

According to one embodiment, the resin phase further comprises at least one **polymerization inhibitor**.

In one embodiment, the polymerization inhibitor is a phenolic antioxidant with at least one function suitable for catalysing the degradation of peroxy radicals such as phenol. In
25 one specific embodiment, the polymerization inhibitor is selected from 3,5-di-tert-4-butylhydroxytoluene (BHT) [CAS number 128-37-0], 4-methoxyphenol and 2,2,4,4-tetramethylpiperidiny-1-oxyl. In one more specific embodiment, the polymerization inhibitor is 3,5-di-tert-4-butylhydroxytoluene (BHT).

In one embodiment, the polymerization inhibitor has high biocompatibility. High biocompatibility may for example be characterized by a LD₅₀ higher than 1 g/kg, e.g. ranging from 1 to 10.

In one embodiment, the polymerization inhibitor has a volatility lower than 0.1 Pa at 25°C, e.g. ranging from 0.01 to 0.1 Pa at 25°C.

According to one embodiment, the polymerization inhibitor is present in an amount ranging from 0.0001 % to 0.1 % w/w, in weight by total weight of the resin phase.

According to one embodiment, the **micro fillers** are mixed oxide glass particles.

According to one embodiment, the micro fillers are mixed oxide glass particles with a “high fraction” of heavy metals, i.e. containing a fraction higher than 25 % w/w, in weight by weight of the micro fillers, of oxides from metals or metalloids with a density higher than 2.5 g/cm³.

According to one embodiment, the micro fillers are surface-coated with a vinyl monomer. In one embodiment, the micro fillers are surface-coated with an acrylate and/or methacrylate monomer, e.g. 3-(trimethoxysilyl)propyl methacrylate.

According to one embodiment, the micro fillers have a particle size lower than or equal to 10 µm. In one embodiment, the micro fillers have a particle size ranging from 10 µm to 0.1 µm. In one embodiment, the micro fillers have a particle size lower than or equal to 5 µm. In one specific embodiment, the micro fillers have a particle size higher than or equal to 1 µm.

According to one embodiment, the micro fillers are amorphous.

According to one embodiment, the micro fillers have a bimodal size distribution, e.g. two regimes, one centred around 1 µm and another around 10 µm.

In one embodiment, the micro fillers are micro glass particles SCHOTT® (G018-307) [similar to CAS number 65997-17-3] or micro glass particles ESSTECH® (EEG 103-3 or EEG 10) [similar to CAS number 65997-17-3].

According to one embodiment, the micro fillers have a refractive index lower than 1.55.
In one embodiment, the micro fillers have a refractive index lower than 1.52.

According to one embodiment, the micro fillers are radioopaque.

5 The micro fillers are preferably present in an amount ranging from 25% to 99.9% w/w, in weight by total weight of the inorganic phase. According to one embodiment, the micro fillers are present in an amount ranging from 60% to 99% w/w. In one embodiment, the micro fillers are present in an amount ranging from 65% to 99% w/w, e.g. ranging from 70% to 80% w/w, ranging from 75% to 85% w/w, ranging from 80% to 90% w/w, ranging from 85% to 95% w/w, or ranging from 90% to 99% w/w.

10 According to one embodiment, the **nano fillers** comprise silica. According to one embodiment, the nano fillers comprise super fine glass particles (approx. 100 nm).

According to one embodiment, the nano fillers are surface-coated with a vinyl monomer. In one embodiment, the nano fillers are surface-coated with an acrylate and/or methacrylate monomer, e.g. 3-(trimethoxysilyl)propyl methacrylate.

15 According to one embodiment, the nano fillers are amorphous.

According to one embodiment, the nano fillers have a particle size lower than or equal to 100 nm. In one embodiment, the nano fillers have a particle size ranging from 100 nm to 0.1 nm. In one embodiment, the nano fillers have a particle size lower than or equal to 10 nm. In one specific embodiment, the nano fillers have a particle size higher than or
20 equal to 1 nm.

In one embodiment, the nano fillers are nano silica Aerosil® (R7200, Evonik). In one embodiment, the nano fillers are SCHOTT® submicron grind glass particles (NF 180, G018-308, Schott).

25 The nano fillers are preferably present in an amount ranging from 0.1% to 75% w/w, in weight by total weight of the inorganic phase. According to one embodiment, the nano fillers are present in an amount ranging from 1% to 40% w/w. In one embodiment, the nano fillers are present in an amount ranging from 1% to 35% w/w, e.g. ranging from 1%

to 10% w/w, ranging from 5% to 15% w/w, ranging from 10% to 20% w/w, ranging from 15% to 25% w/w, or ranging from 20% to 30% w/w.

According to one embodiment, the formulation further comprises at least one **pigment**.

In one embodiment, the pigment is in the resin phase. In one embodiment, the pigment is
5 in the inorganic phase.

In one embodiment, the pigment is an inorganic pigment. In one embodiment, the pigment is selected from zinc/iron oxide, iron oxide, iron/chromium oxide, titanium dioxide, and mixtures thereof.

In one embodiment, the pigment is present in an amount ranging from 0.0001% to
10 0.01% w/w, in weight by total weight of the inorganic phase.

According to one embodiment, the formulation further comprises **additional components** such as for example antioxidants, antimicrobials, buffers, chelating agents, pH adjusters, preservatives, solubilizers, stabilizers, surfactants, thickening agents, viscosity modulator agents or mixtures thereof.

15 According to one embodiment, the formulation is a cosmetic composition. According to one embodiment, the formulation is a pharmaceutical composition.

According to one embodiment, the composite formulation is free of bisphenol A glycerolate dimethacrylate (BisGMA). According to one embodiment, the composite formulation is free of triethylene glycol dimethacrylate (TegDMA). In one embodiment,
20 the composite formulation is free of BisGMA and TegDMA.

The formulation according to the invention is especially advantageous because it is a “fast-curing” formulation. The formulation may be cured in 10 seconds or less, typically in 5 seconds or less, when irradiated at a wavelength ranging from 380 to 450 nm (purple), i.e. the curing time is about 3-fold lower, typically about 5-fold lower, with the
25 formulation of the invention compared to conventional composites.

The formulation according to the invention is also especially advantageous because it allows complete polymerization of the resin phase at clinically acceptable depths (about 2 mm). The degree of polymerization may reach 75-80 % when irradiated at a wavelength ranging from 380 to 450 nm (purple), i.e. more than the degree of polymerization of conventional composites (50-65% typical).

The formulation according to the invention is also especially advantageous because it allows homogeneous polymerization of the resin phase at clinically acceptable depths (about 2 mm).

The formulation according to the invention is also especially advantageous because it is easy to handle for a dental practitioner due to its volume stability (non-flowing), its non-stick texture and sculptability (retains a given shape).

This invention also relates to a **composite material** resulting from the cure of a composite formulation as previously described.

The cure is obtained by means of the polymerization of the resin phase.

The material according to the invention is also especially advantageous because it has high mechanical properties, at least equivalent to those of conventional composite materials. Mechanical properties may for example be characterized by surface hardness, flexural modulus and flexural strength. Hardness can be measured, for example, as disclosed in Example 1 below. The flexural modulus and flexural strength can be measured using a stain-stress testing equipment equipped with a 3- or 4-point flexure jig.

The material according to the invention is also especially advantageous because it has high chemical stability, at least equivalent to the stability of conventional composite materials. Chemical stability may for example be characterized by measuring solvent sorption and mass variation over time. This can be done by immersing a material in an aqueous medium and following changes of mass over time, taking the initial dry mass and final dry mass as references.

The invention also relates to a **process for manufacturing a composite formulation**, especially a composite formulation according to the invention as described hereabove.

According to one embodiment, the manufacturing process comprises:

- (a) Mixing a first, second, third and fourth monomers so as to obtain a resin blend;
- (b) Adding and dispersing in the resin blend obtained at step (a) a photoinitiator and optionally at least one polymerization inhibitor as powders, so as to obtain the resin phase of the formulation; and
- (c) Adding and dispersing in the resin phase obtained at step (b) nano fillers, then micro fillers, and then optionally at least one pigment, so as to obtain the formulation.

In one embodiment, step (a) is carried out at room temperature.

- 10 The invention also relates to a **process for manufacturing a composite material**, especially a composite material according to the invention as described hereabove.

According to one embodiment, the manufacturing process comprises:

- (A) Providing a composite formulation according to the invention as described hereabove; and
 - (B) Photopolymerizing the formulation by applying artificial light, so as to cure said formulation,
- thereby obtaining said material.

In one embodiment, the artificial light has a wavelength ranging from 380 to 450 nm (near-UV, purple). In one specific embodiment, the artificial light has a wavelength ranging from 400 to 410 nm.

In one embodiment, the artificial light has a high intensity, i.e. an intensity of at least 1000 mW/cm², e.g. ranging from 1000 to 2000 mW/cm². In one specific embodiment, the artificial light has a high intensity ranging from 1000 to 1500 mW/cm².

In one embodiment, the artificial light is applied for a duration ranging from 0.5 to 50 seconds, preferably from 1 to 25 seconds. In one specific embodiment, the artificial

light is applied for a duration ranging from 1 to 11 seconds, e.g. ranging from 2 to 6 seconds, from 3 to 7 seconds, from 4 to 8 seconds, from 3 to 9 seconds or from 4 to 10 seconds.

In one embodiment, the process further comprises an additional step (A-1) between step
5 (A) and (B), said step (A-1) consisting in applying said formulation into and/or onto a tooth.

The formulation and/or the material according to the invention is/are especially useful in the field of dentistry.

The invention also relates to a formulation according to the invention as described
10 hereabove and/or to a material according to the invention as described hereabove, for use as a medicament. According to one embodiment, the formulation and/or the material is for use in the treatment of a tooth disease or damage.

The invention also relates to a method of dental treatment comprising applying a formulation according to the invention as described hereabove and/or a material
15 according to the invention as described hereabove into and/or onto the tooth of a subject in need thereof. According to one embodiment, the formulation and/or the material is used in the method as a restorative material.

The invention also relates to the use of a formulation according to the invention as described hereabove or the material according to the invention as described hereabove in
20 the manufacture of a dental composite.

Any reference to a “**tooth**” or “**dental treatment**” or “**dentistry**” in the present patent application shall not be constructed as being limited to living organisms or *in vivo* procedures. The present invention includes for example the application of a dental composite onto and/or into three-dimensional tooth and/or jaw models; and any *ex vivo*
25 dentistry procedure where a dental composite may be used.

Any reference to a “**tooth**” or “**dental treatment**” or “**dentistry**” in the present patent application shall not be constructed as being limited to therapeutic use. The present

invention includes for example the use of dental composite for cosmetic, artistic or recreative purposes.

BRIEF DESCRIPTION OF THE DRAWINGS

5 **Figure 1** is a graph showing the Vickers hardness number (VHN) (HV0.2/30) of **Formulation 1** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

Figure 2 is a graph showing the percentage of the maximal VHN (%) of **Formulation 1**
10 in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

Figure 3 is a graph showing the Vickers hardness number (VHN) (HV0.2/30) of **Formulation 2** in different curing time(s), as described in **Example 1** below. The grey
15 curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

Figure 4 is a graph showing the percentage of the maximal VHN (%) of **Formulation 2** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve shows
20 (square dots) the VHN measured at the bottom of the sample.

Figure 5 is a graph showing the Vickers hardness number (VHN) (HV0.2/30) of **Formulation 3** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

25 **Figure 6** is a graph showing the percentage of the maximal VHN (%) of **Formulation 3** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

Figure 7 is a graph showing the Vickers hardness number (VHN) (HV0.2/30) of **Formulation 4** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

- 5 **Figure 8** is a graph showing the percentage of the maximal VHN (%) of **Formulation 4** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

- 10 **Figure 9** is a graph showing the Vickers hardness number (VHN) (HV0.2/30) of **Formulation 5** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

- 15 **Figure 10** is a graph showing the percentage of the maximal VHN (%) of **Formulation 5** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

- 20 **Figure 11** is a graph showing the Vickers hardness number (VHN) (HV0.2/30) of **Formulation 6** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

Figure 12 is a graph showing the percentage of the maximal VHN (%) of **Formulation 6** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

- 25 **Figure 13** is a graph showing the Vickers hardness number (VHN) (HV0.2/30) of **Formulation 7** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

Figure 14 is a graph showing the percentage of the maximal VHN (%) of **Formulation 7** in different curing time (s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

- 5 **Figure 15** is a graph showing the Vickers hardness number (VHN) (HV0.2/30) of **Formulation 8** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

- 10 **Figure 16** is a graph showing the percentage of the maximal VHN (%) of **Formulation 8** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

- 15 **Figure 17** is a graph showing the Vickers hardness number (VHN) (HV0.2/30) of **Formulation 9** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

- 20 **Figure 18** is a graph showing the percentage of the maximal VHN (%) of **Formulation 9** in different curing time(s), as described in **Example 1** below. The grey curve (circular dots) shows the VHN measured at the top of the sample, whereas the black curve (square dots) shows the VHN measured at the bottom of the sample.

EXAMPLES

The present invention is further illustrated by the following example.

Example 1: Formulations according to the invention and properties thereof

- 25 Hereafter are presented examples of formulations according to the invention, wherein each resin phase is a blend of four different monomers comprising a sensitizer.

The resin phase composition is as shown in **Table 1** below (in weight by weight of the total weight of the resin phase):

Composition (% w/w)	1	2	3	4	5
Urethane dimethacrylate (UDMA)	35.0	80.0	70.0	50.0	50.0
Tricyclodecane dimethanol diacrylate (TCCDA)	30.0	10.0	10.0	10.0	-
N-Benzylmethacrylamide (N-BMA)	-	-	-	-	10.0
Ethylene glycol dicyclopentenyl ether acrylate (EGDCPEA)	-	-	-	-	-
1,6-Hexanediol dimethacrylate (HDDMA)	25.0	5.0	10.0	-	30.0
1,6-Hexanediol diacrylate (HDDA)	-	-	-	-	-
Trimethylolpropane trimethacrylate (TMPTMA)	-	-	-	30.0	-
Poly(ethylene glycol) dimethacrylate (PegDMA), Mn 750	9.5	4.5	8.0	9.5	9.5
Poly(ethylene glycol) diacrylate (PegDA), Mn 575	-	-	-	-	-
Diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (TPO)	0.5	0.5	2.0	0.5	0.5
Phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide	-	-	-	-	-

Table 1

Composition (% w/w)	6	7	8	9
Urethane dimethacrylate (UDMA)	60.0	50.0	50.0	60.0
Tricyclodecane dimethanol diacrylate (TCCDA)	-	-	-	-
N-Benzylmethacrylamide (N-BMA)	10.0	10.0	-	10.0
Ethylene glycol dicyclopentenyl ether acrylate (EGDCPEA)	-	-	20.0	-
1,6-Hexanediol dimethacrylate (HDDMA)	-	-	-	-
1,6-Hexanediol diacrylate (HDDA)	20.0	-	-	20.0
Trimethylolpropane trimethacrylate (TMPTMA)	-	20.0	10.0	-
Poly(ethylene glycol) dimethacrylate (PegDMA), Mn 750	9.5	-	-	9
Poly(ethylene glycol) diacrylate (PegDA), Mn 575	-	19.0	19.0	-
Diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (TPO)	0.5	1.0	1.0	-
Phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide	-	-	-	1.0

Table 1 (continued)

The inorganic phase composition is as shown in **Table 2** below (in weight by weight of the total weight of the inorganic phase):

Composition (% w/w)	1	2	3	4	5
Micro glass particles SCHOTT® (K6 grind, G018-307)	92.3	92.3	-	92.3	92.3
Micro glass particles ESSTECH® (EEG 103-3)	-	-	91.7	-	-
Nano silica Aerosil® (R7200)	7.7	7.7	8.3	7.7	7.7

Table 2

Composition (% w/w)	6	7	8	9
Micro glass particles SCHOTT® (K6 grind, G018-307)	92.3	92.3	92.3	92.3
Micro glass particles ESSTECH® (EEG 103-3)	-	-	-	-
Nano silica Aerosil® (R7200)	7.7	7.7	7.7	7.7

Table 2 (continued)

Resin phase represents 35% w/w and inorganic phase 65% w/w in Formulations **1, 2, 4, 5, 6, 7, 8** and **9**; and resin phase represents 40% w/w and inorganic phase 60% w/w in Formulation **3**; in weight by weight of the total weight of the formulation.

- 5 All Formulations **1-5** further includes 0.1 mg of Habirox Yellow 9310 pigment (Habich GmbH, Germany).

Materials and Methods

Material

- 10 Chemicals were purchased from commercial sources and used without further purification.

- All light curing steps were carried out using a commercially available light source (AURA light engine, Lumencor). The light source features independently selectable outputs, namely either the “violet” or “blue” mode (405 or 470 nm, respectively for λ_{max}). The light intensity was controlled using the dedicated software interface and was calibrated to
 15 1000 mW/cm² using a thermal sensor (S370C connected to a personal computer with a dedicated software, Thorlabs) – measured at the exit. The diameter of the light guide was 5 mm.

Methods – Manufacturing process

- 20 The manufacture was carried out under a filtered light environment (longpass filter, higher than 500 nm) with clean utensils and taking care to avoid contamination (protective gear including gloves, hat and mask).

When a component under a powder form show visible aggregates, the powder is grinded

manually using a pestle and mortar prior to its addition to the mixture.

The monomers were added at room temperature (approx. 20 °C) in a container and mixed using a centrifuge or a mechanical stirrer.

5 The photoinitiator was then added as a powder and dispersed to the resin using a centrifuge or mechanical stirrer until the powder was no longer visible in the resin blend, taking care not to overheat the mixture (step mixing cycles if required).

The inhibitor may be added if long-term storage is expected. Inhibitor powder is then added and dispersed as with the photoinitiator.

10 If the mixing was carried out under atmospheric pressure, remove entrapped air with a static vacuum chamber (for example at 0.1 bar for 10 to 60 minutes).

The nano fillers were then added as particles to the resin and introduced therein by mixing with increasing energy (reach mild vacuum before mixing).

When maximized particle wetting by the resin phase is desired, then the mixture may be left to rest for 24 hours.

15 The micro fillers were then added as particles to the mixture and introduced therein by mixing at low energy, taking care not to overheat the mixture (step mixing cycles is required).

The pigment was then added and mixed until a homogeneous shade is reached (may require several shorter mixing cycles to avoid overheating).

20 The resulting formulation was stored at 4 °C in a lightproof container and low humidity environment until further use.

Methods – Manufacture of the composite material

25 The material was placed as a paste in a white Teflon cylindrical split mold (2 mm high and 5 mm diameter). The mold upper and lower surfaces were then covered with a mylar sheet, the mold pressed with a hand press.

The uncured material was then illuminated for 1-6 seconds, 8 or 10 seconds using the violet mode, emitting at 405 nm ($n = 2$), with the light tip in contact with the mylar sheet. Following illumination, a specimen was removed from the mold and the upper surface was identified.

- 5 Following illumination, specimens were stored for at least 24h at room temperature in the dark before analysis.

Methods – Microhardness measurement

- Vickers measurements were carried out on the upper and lower surfaces using a Durimet microhardness tester (Leitz, Germany); at room temperature (20-23 °C), ambient
10 humidity (40-70 %) and daylight with neon lighting. A load of 200 g was applied for 30 seconds on the surface, the length of the diagonal of each indentation was measured directly using a graduated eye-lens.

- The Vickers hardness number (VHN) was obtained using tables, based on the following equation (average of 2 indents per specimen): $H = 1.8544 (P.d^{-2})$, where P is the
15 magnitude of the force exerted in kilogram-force, d is the length of the diagonal in millimetres and H is the Vickers hardness.

Results

Formulations 1-9 and composite materials thereof were successfully manufactured according to the methods described hereinbelow.

- 20 Measurement of hardness corresponds to the resistance to plastic deformation under the stress produced by a small-sized indenter. The higher the hardness value, the more rigid the material. Hardness reflects the state of the resin phase of the composite: increasing crosslinking and curing are associated with increasing hardness. Hardness measurement at the top and bottom surfaces of a specimen of composite material is a means to
25 investigate the homogeneity of curing through depth. Small differences in hardness between upper and lower surfaces may occur due to the geometry of the setup (increased reflection at the top of the mold).

All Formulations **1-9** were fully cured after 3 to 5 seconds as shown in **Figures 1-18** and in **Table 3** below.

Mean hardness is calculated as the mean of measured hardness for 8s and 10s specimens.

	Thickness (mm)	Full curing time(s)	Mean hardness (HV0.2)	
Formulation 1	2	5	Top	42.7
			Bottom	43.1
Formulation 2	2	3	Top	41.3
			Bottom	45.4
Formulation 3	2	5	Top	36.8
			Bottom	41.3
Formulation 4	2	5	Top	46.5
			Bottom	49.3
Formulation 5	2	4	Top	23.5
			Bottom	30.8

Table 3

	Thickness (mm)	Full curing time(s)	Mean hardness (HV0.2)	
Formulation 6	2	2	Top	49.2
			Bottom	50.6
Formulation 7	2	5	Top	58.7
			Bottom	65.3
Formulation 8	2	3	Top	51.7
			Bottom	51.6
Formulation 9	2	3	Top	47.7
			Bottom	58.6

5

Table 3 (continued)

There results unambiguously show that **Formulations 1-9** allows the manufacture of dental composite material having good mechanical properties with clinically acceptable thickness in fast curing time. Curing time is 5 seconds or less, i.e. 5-fold lower than commercial dental formulations.

- 10 Therefore, the novel formulations according to the invention overcome the limitations of prior art dental formations.

CLAIMS

1. A formulation comprising a resin phase and an inorganic phase, wherein:

said resin phase comprises:

- 5 - a first monomer selected from vinyl monomers comprising at least one hydroxyl or urethane group;
- a different second monomer selected from vinyl monomers having a molecular weight higher than 300 g/mol, a refractive index ranging from 1.5 to 1.7, and a viscosity higher than 1 Pa.s at 25°C;
- 10 - a different third monomer selected from vinyl monomers having a molecular weight lower than 300 g/mol, a viscosity lower than 1 Pa.s at 25°C, and a log P higher than 3;
- a different fourth monomer selected from vinyl monomers comprising at least one polyether group;
- a photoinitiator having:
 - 15 a molar absorptivity higher than $100 \text{ L.mol}^{-1}.\text{cm}^{-1}$ at a spectral wavelength ranging from 380 to 450 nm,
 - a quantum yield of alpha-cleavage higher than 0.5 in acetonitrile at a spectral wavelength ranging from 380 to 450 nm, and
 - a solubility higher than 50 g/L in trimethylpropane triacrylate
- 20 at 25°C; and
- optionally, at least one polymerization inhibitor; and

said inorganic phase comprises

- micro fillers, preferably mixed oxide glass particles, having a particle size ranging from 1 μm to 10 μm and a refractive index lower than 1.55;
- 25 - nano fillers, preferably amorphous silica, having a particle size ranging from 1 nm to 100 nm, and
- optionally, at least one inorganic pigment.

2. The formulation according to claim 1, wherein said resin phase is present in an amount ranging from 5% to 60% w/w and the inorganic phase is present in an amount ranging from 40% to 95% w/w, in weight by weight of the total weight of the formulation.
- 5 3. The formulation according to claim 1 or claim 2, wherein said first monomer is selected from acrylates, methacrylates and acrylamides substituted by at least one hydroxyl or urethane group; preferably said first monomer is selected from diurethane dimethacrylate, 1,3-glyceryl dimethacrylate, polycarbonate dimethacrylate, 3-phenoxy-2-hydroxypropyl-methacrylate, 2-hydroxy-3-phenoxypropyl acrylate, (3-hydroxy-1-adamantyl) 2-methylprop-2-enoate, 10 N,N'-ethylenebis(acrylamide), N,N'-(1,2-dihydroxyethylene)bisacrylamide and pre-reacted oligomers thereof.
4. The formulation according to any one of claims 1 to 3, wherein said second monomer is selected from acrylates, methacrylates and acrylamides comprising at least one group selected from phenyl, xylyl, naphthyl and combinations thereof; 15 preferably said second monomer is selected from tricyclodecane dimethanol diacrylate, N-benzylmethacrylamide, phenyl methacrylate, benzyl methacrylate, 2,2',6,6'-tetrabromo bisphenol A dimethacrylate, 2-phenoxyethyl methacrylate, cyclic trimethylol-propane formal acrylate, 2,4,6-tribromophenyl acrylate and 20 ethylene glycol dicyclopentenyl ether acrylate.
5. The formulation according to any one of claims 1 to 4, wherein said third monomer is selected from acrylates, methacrylates and acrylamides wherein the acrylate, methacrylate and/or acrylamide functions are separated by at least one alkylene backbone; preferably one C₅-C₁₀ alkylene backbone; preferably said third monomer 25 is selected from 1,6-hexanediol dimethacrylate, trimethylolpropane trimethacrylate, 1,3-propanediol dimethacrylate, 1,4-butanediol dimethacrylate, 1,10-decanediol dimethacrylate, 1,12-dodecanediol dimethacrylate, pentaerythritol tetramethacrylate, 1,6-hexanediol diacrylate, 1,4-butanediol diacrylate, 1,10-decanediol diacrylate, 1,12-dodecanediol diacrylate, pentaerythritol 30 tetraacrylate, N,N'-hexamethylenebis(methacrylamide) and trimethylolpropane

propoxylate triacrylate.

6. The formulation according to any one of claims 1 to 5, wherein said fourth monomer is selected from acrylates, methacrylates and acrylamides comprising at least one polyether group; preferably said fourth monomer is selected from tetraethylene glycol dimethacrylate, poly(ethylene glycol) methacrylates comprising at least two methacrylate groups and poly(ethylene glycol) diacrylamides; more preferably from poly(ethylene glycol) dimethacrylate and poly(ethylene glycol) diacrylate.
7. The formulation according to any one of claims 1 to 6, wherein said photoinitiator is selected from organophosphine oxides; preferably said photoinitiator is selected from diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide, bis(2,6-dimethoxybenzoyl)-2,4,4-trimethylpentyl phosphine oxide and phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide.
8. The formulation according to any one of claims 1 to 7, wherein said first monomer is present in an amount ranging from 25% to 75% w/w, said second monomer is present in an amount ranging from 1% to 50% w/w, said third monomer is present in an amount ranging from 1% to 50% w/w, said fourth monomer is present in an amount ranging from 1% to 25% w/w and said photoinitiator is present in an amount ranging from 0.01% to 2.5% w/w, in weight by total weight of the resin phase.
9. The formulation according to any one of claims 1 to 8, wherein said micro fillers are present in an amount ranging from 60% to 99% w/w and said nano fillers are present in an amount ranging from 1% to 40% w/w, in weight by total weight of the inorganic phase.
10. The formulation according to any one of claims 1 to 9, wherein said formulation is free of bisphenol A glycerolate dimethacrylate and/or triethylene glycol dimethacrylate.

11. A material resulting from the cure of a formulation according to any one of claims 1 to 10.
12. A process for manufacturing a formulation according to any one of claims 1 to 10, comprising:
- 5 (a) Mixing the first, second, third and fourth monomers so as to obtain a resin blend;
- (b) Adding and dispersing in the resin blend obtained at step (a) the photoinitiator and optionally at least one polymerization inhibitor as powders, so as to obtain the resin phase of the formulation; and
- 10 (c) Adding and dispersing in the resin phase obtained at step (b) the nano fillers, then the micro fillers, and then optionally at least one pigment, so as to obtain said formulation.
13. A process for manufacturing a material comprising:
- (A) Providing a formulation according to any one of claims 1 to 10;
- 15 (A-1) Optionally, applying said formulation into and/or onto a tooth; and
- (B) Photopolymerizing said formulation by applying artificial light at a spectral wavelength ranging from 380 to 450 nm; preferably ranging from 400 to 410 nm; preferably wherein said artificial light has an intensity of at least 1000 mW/cm²; so as to cure said formulation,
- 20 thereby obtaining said material.
14. A formulation according to any one of claims 1 to 10 and/or a material according to claim 11, for use in the treatment of a tooth disease.
15. Use of a formulation according to any one of claims 1 to 10 and/or a material according to claim 11 in the manufacture of a dental composite.

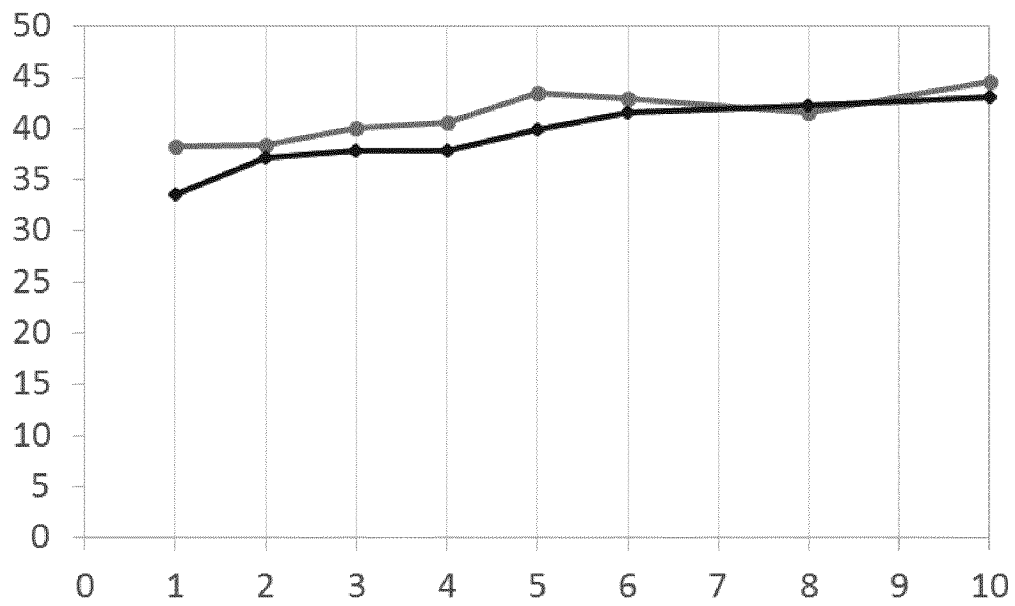


FIG. 1

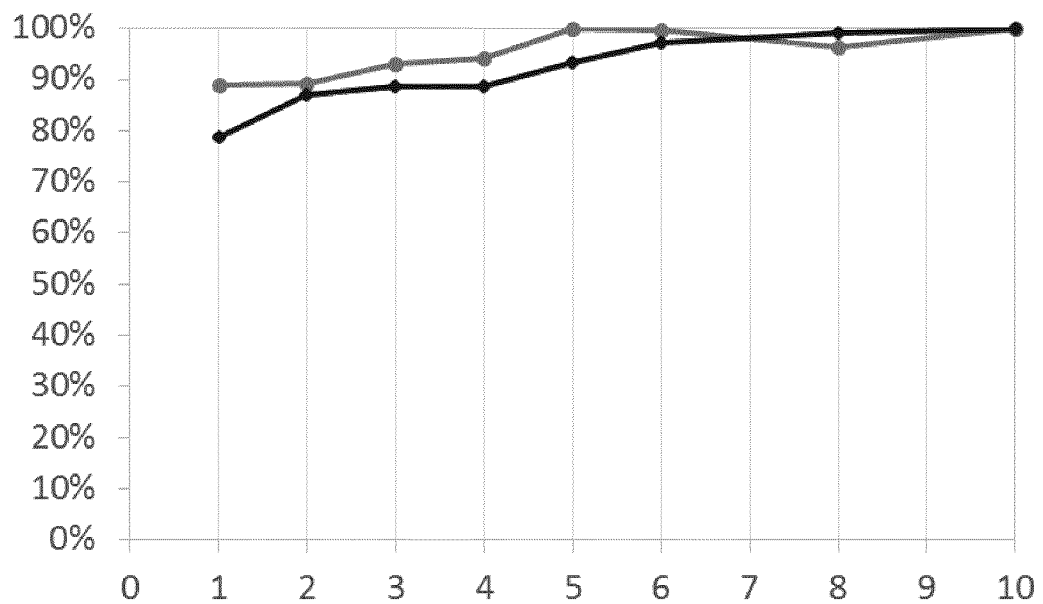


FIG. 2

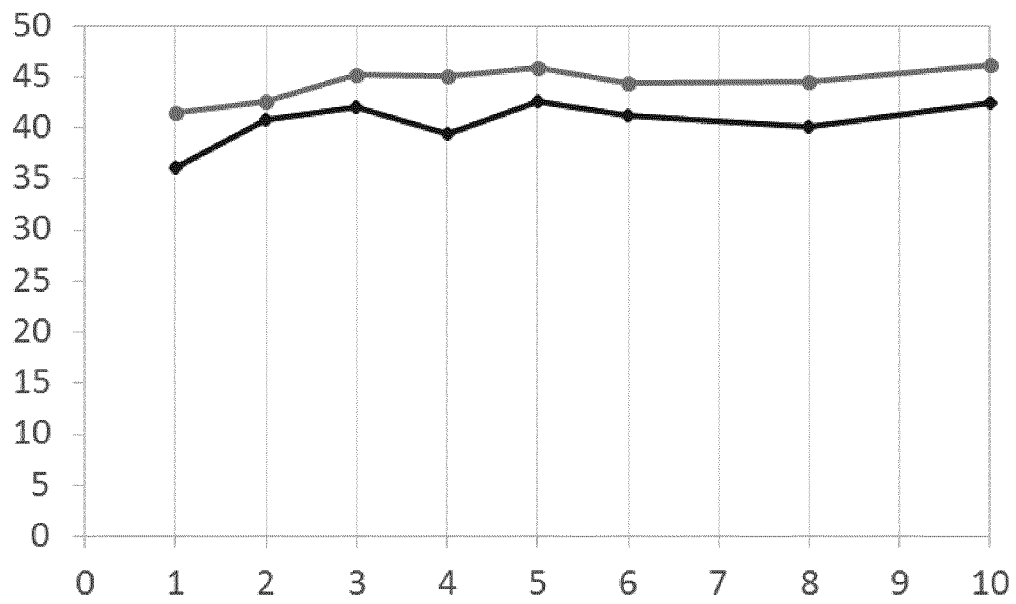


FIG. 3

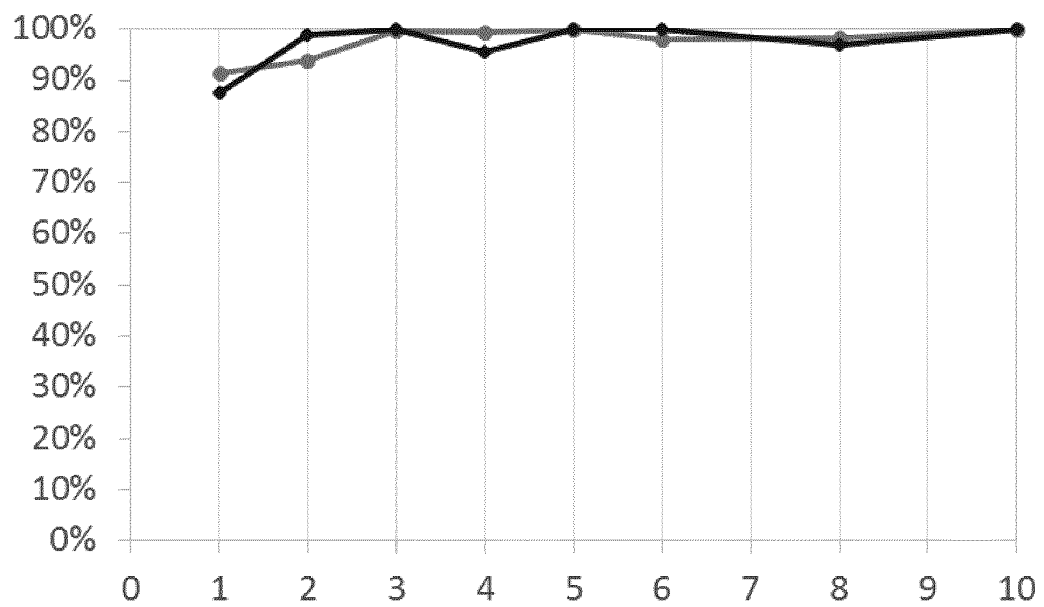


FIG. 4

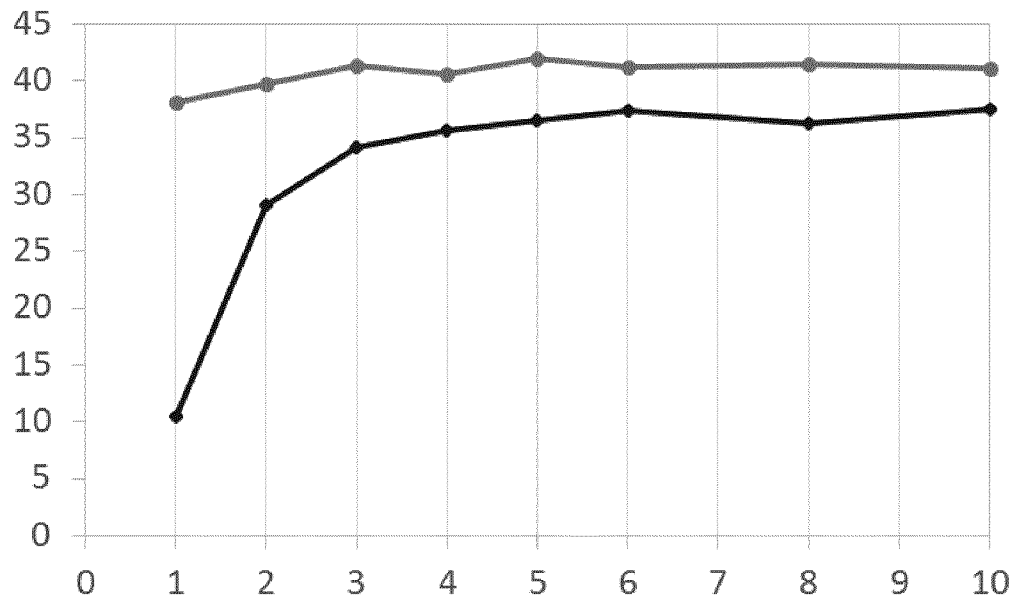


FIG. 5

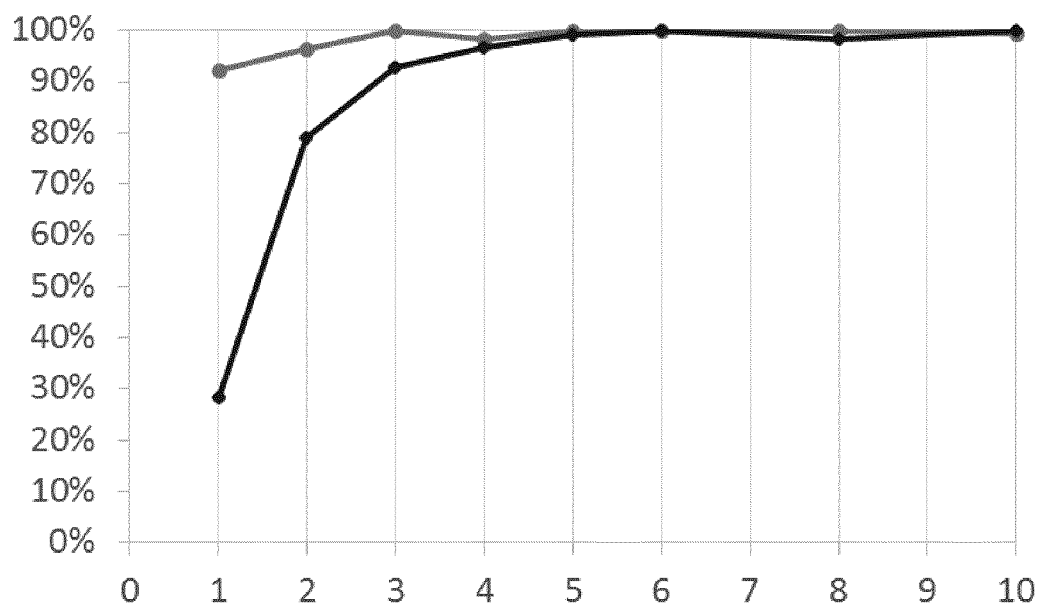


FIG. 6

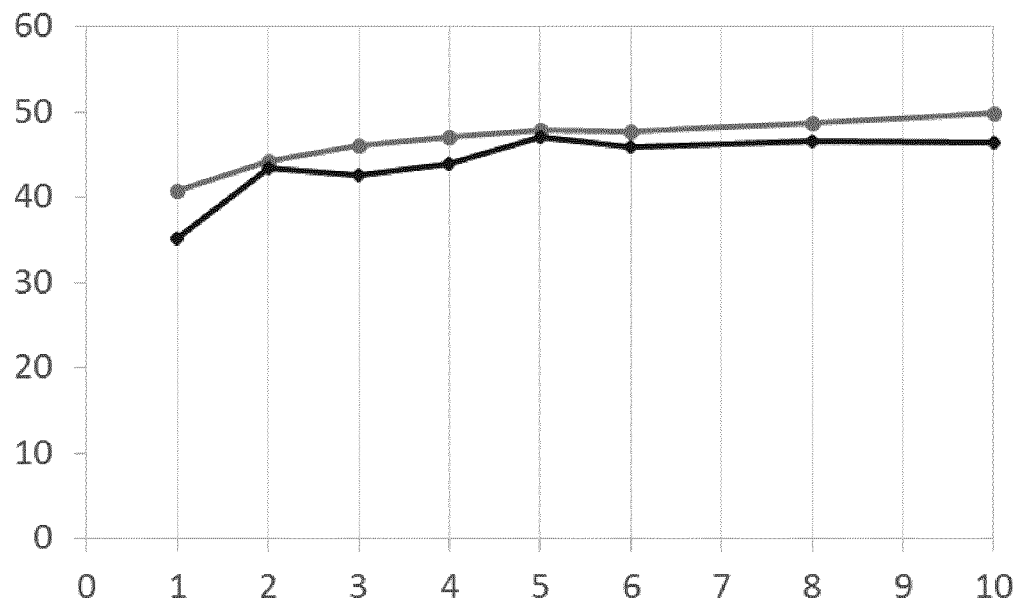


FIG. 7

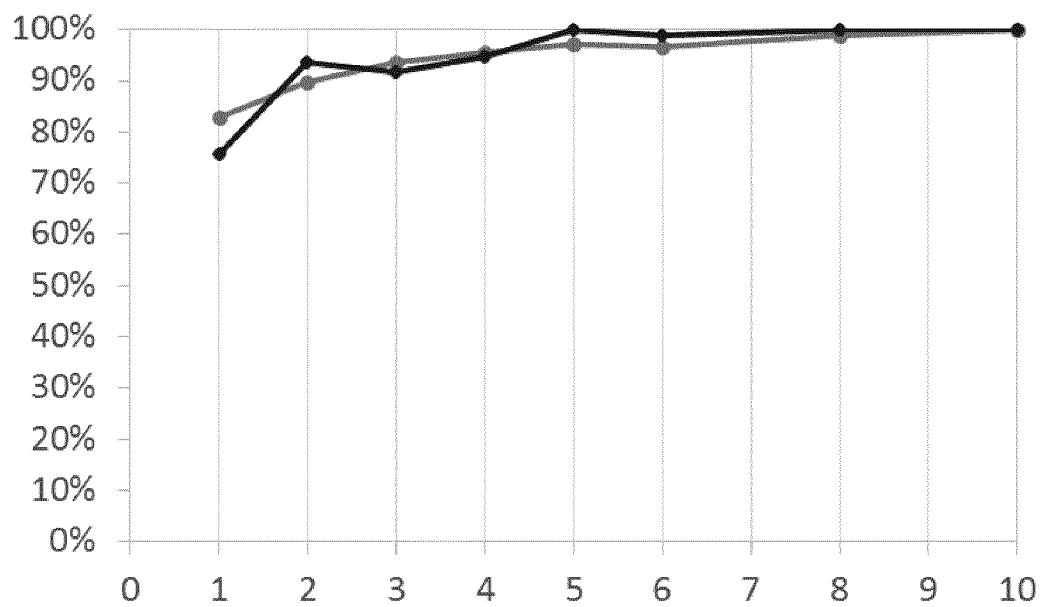


FIG. 8

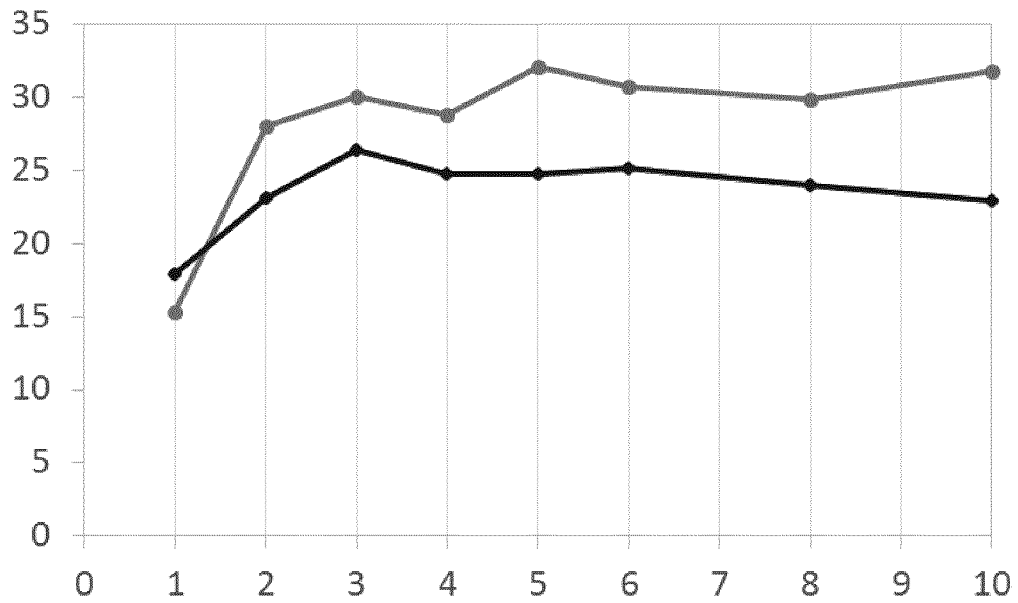


FIG. 9

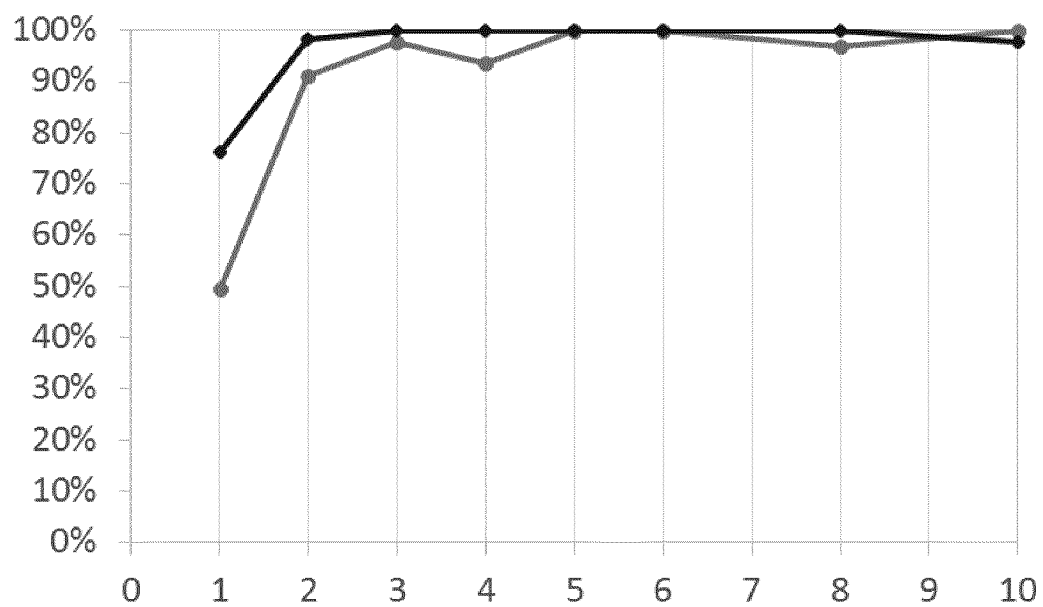


FIG. 10

6/9

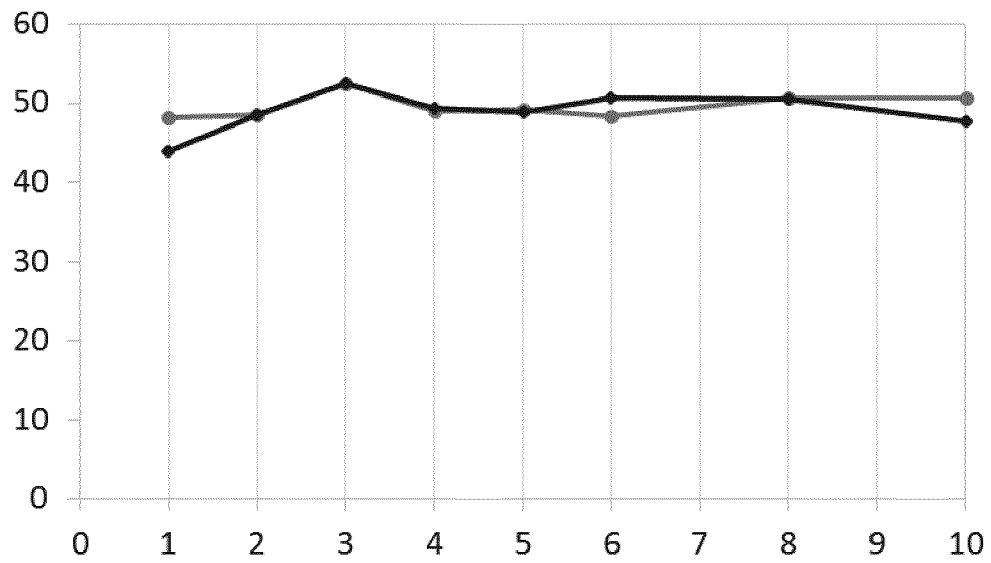


FIG. 11

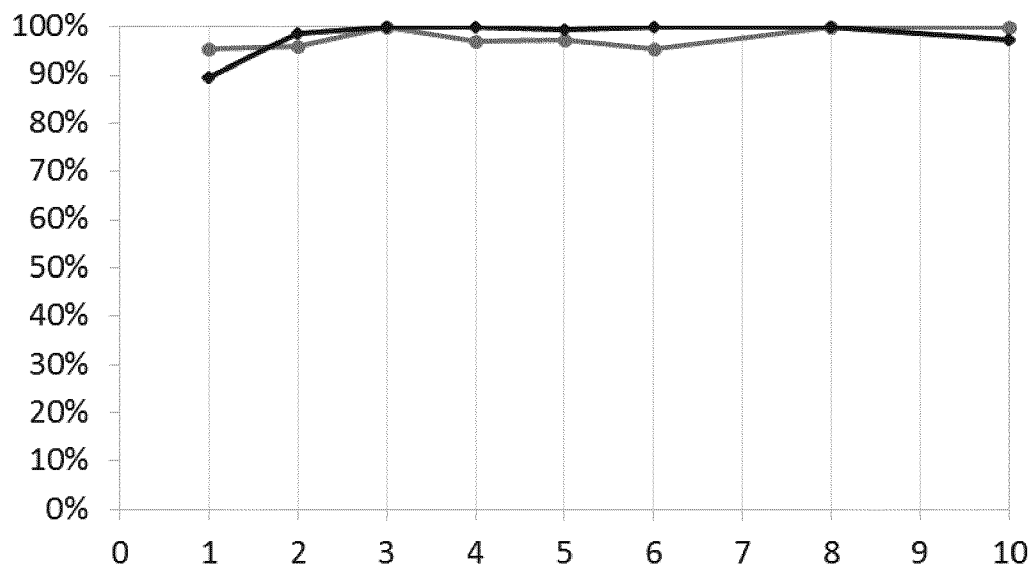


FIG. 12

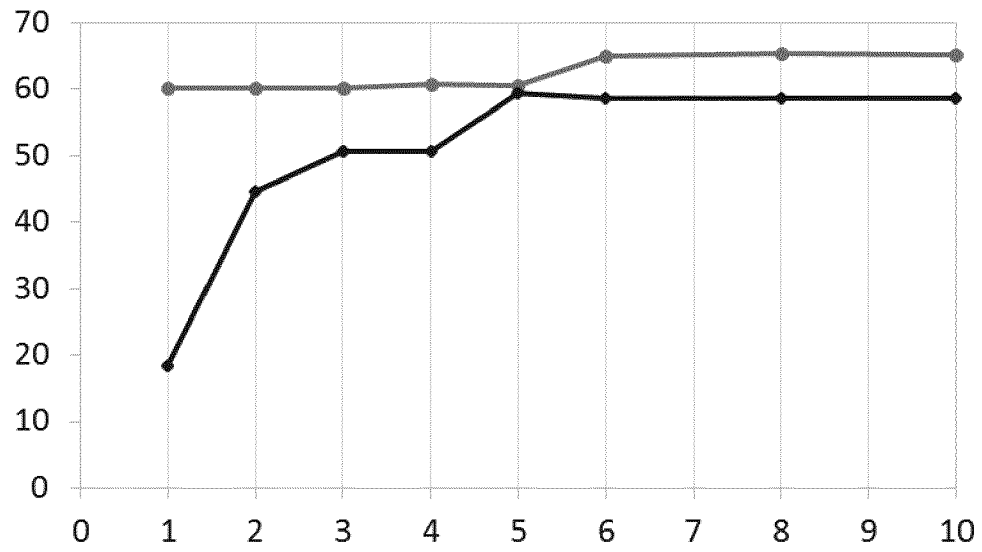


FIG. 13

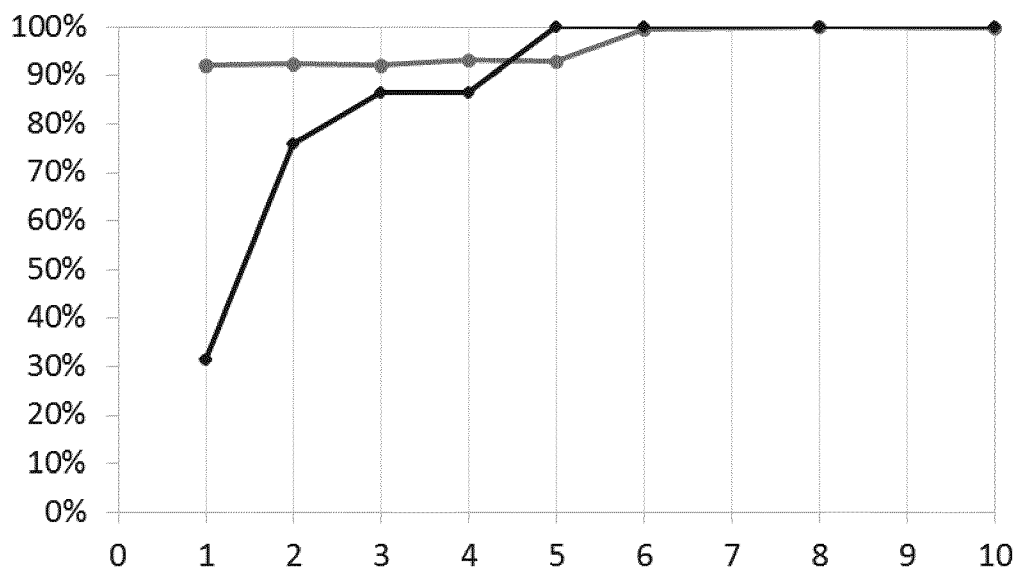


FIG. 14

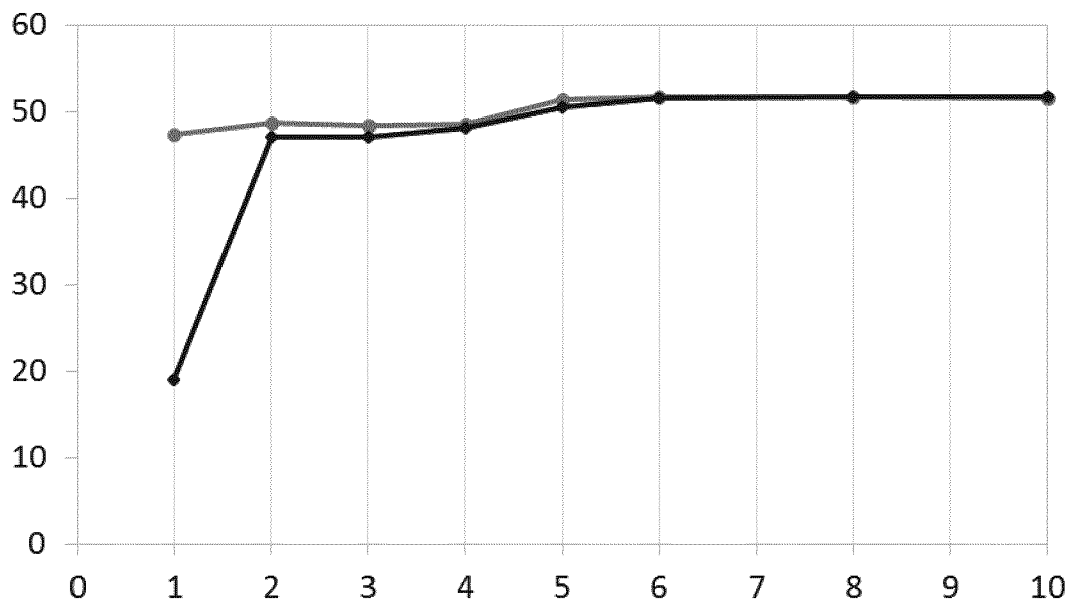


FIG. 15

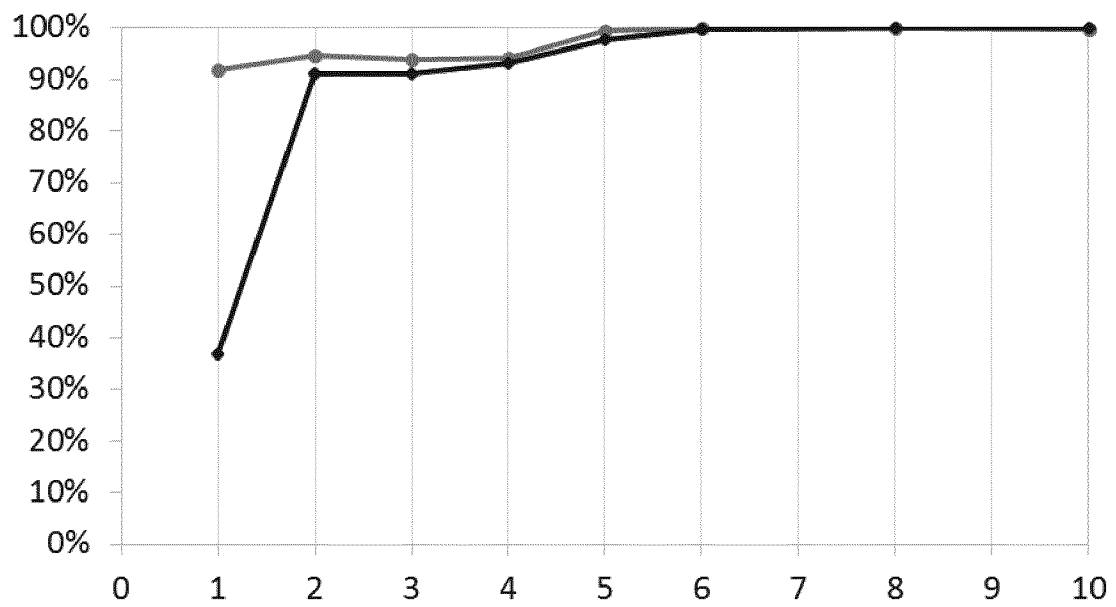


FIG. 16

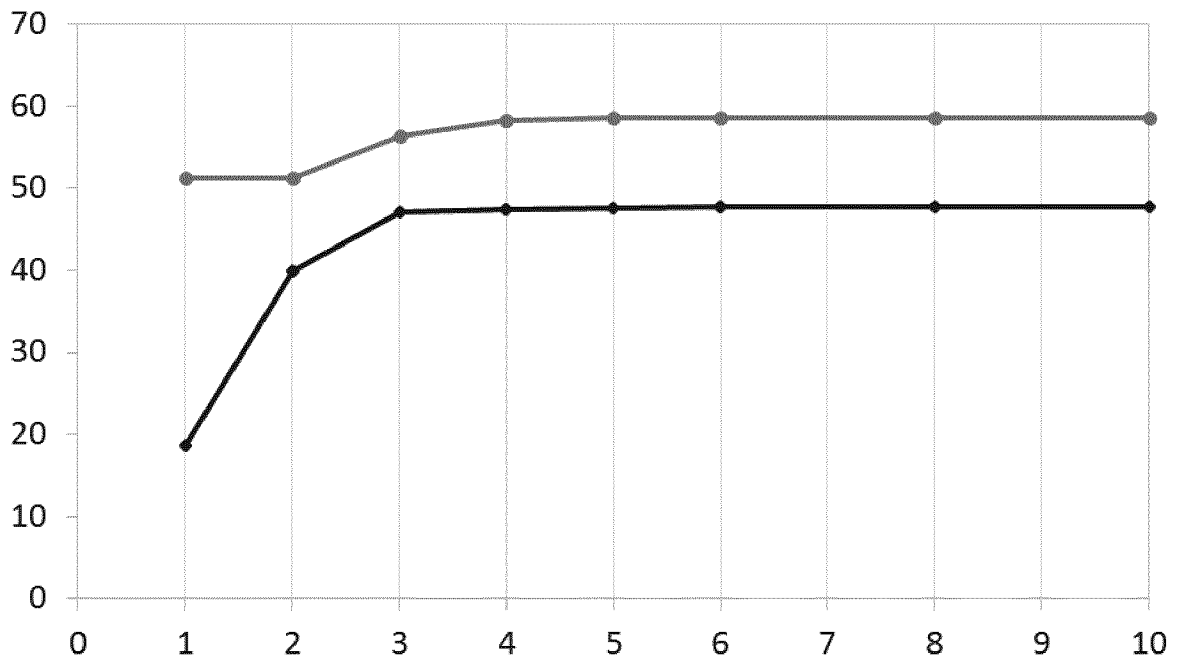


FIG. 17

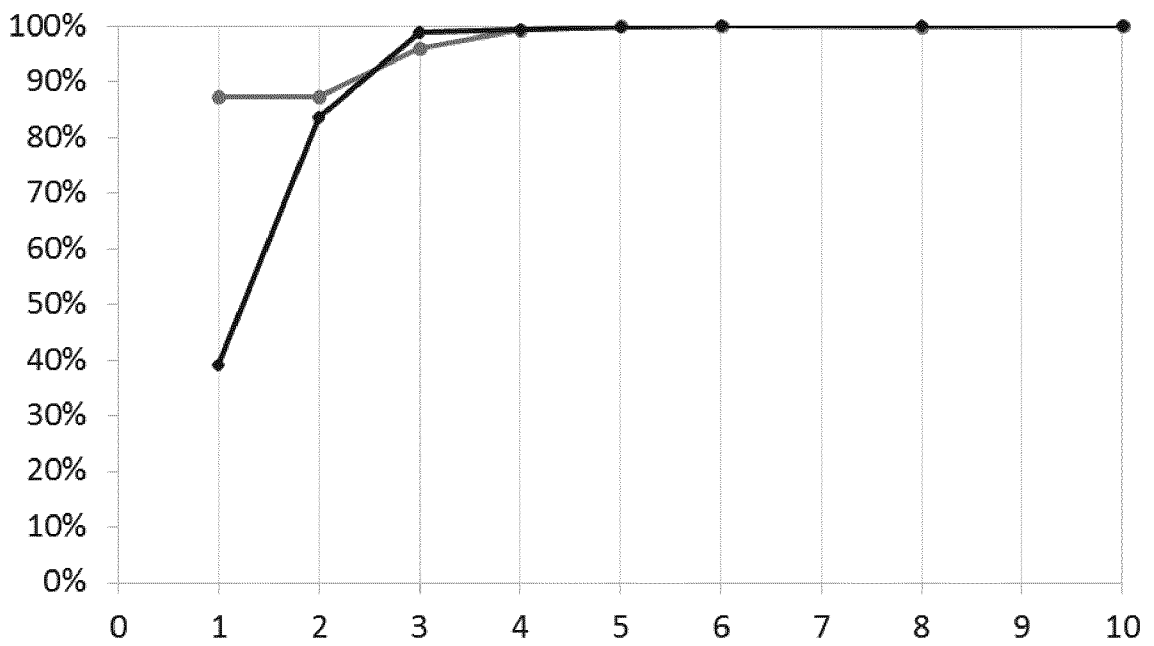


FIG. 18

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2019/083113

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K6/887
ADD.

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)
A61K

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 practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	J. CHESTERMAN ET AL: "Bulk-fill resin-based composite restorative materials: a review", BRITISH DENTAL JOURNAL : BDJ ; THE JOURNAL OF THE BRITISH DENTAL ASSOCIATION, vol. 222, no. 5, 1 March 2017 (2017-03-01) , pages 337-344, XP055604028, UK ISSN: 0007-0610, DOI: 10.1038/sj.bdj.2017.214 table 4	1-15
A	WO 2011/149631 A2 (3M INNOVATIVE PROPERTIES CO [US]; CRAIG BRADLEY D [US] ET AL.) 1 December 2011 (2011-12-01) page 19, line 1 - page 19, line 3; claims; examples ----- -/--	1-15



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

22 January 2020

Date of mailing of the international search report

31/01/2020

Name and mailing address of the ISA/

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Authorized officer

Schmid, Arnold

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2019/083113

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2012/295227 A1 (BOWMAN CHRISTOPHER N [US] ET AL) 22 November 2012 (2012-11-22) paragraph [0077]; claims -----	1-15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2019/083113

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		RU 2012155804 A	27-06-2014
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		WO 2011149631 A2	01-12-2011

US 2012295227 A1	22-11-2012	NONE	
