The examination is being carried out on the **following application documents**

Description, Pages

2-5	as published			
1, 1a	received on	24-02-2012	with letter of	20-02-2012

Claims, Numbers

1-8	received on	16-09-2013	with letter of	11-09-2013

1. Cited documents

1.1. Reference is made to the following documents:

D1 US 2003/082116 A1 (BADEJO ET AL) 1 May 2003

D2 US 6 579 543 B1 (MCCLUNG) 17 June 2003

D3 US 4 877 781 A (LAHAYE ET AL) 31 October 1989

D4 B.E. van Wyk and M. Wink: "Medicinal Plants of the World". Timber Press. Inc., ISBN: 0-88192-602-7, XP002592027, 1 January 2004

D5 QUAVE ET AL: "DERMATOLOGICAL REMEDIES IN THE TRADITIONAL PHARMACOPOEIA OF VULTURE-ALTO BRADANO, INLAND SOUTHERN ITALY"JOURNAL OF ETHNOBIOLOGY AND ETHNOMEDICINE. vol. 4, no. 5, DOI: 10.1186/1746-4269-4-5, XP0025916246, February 2008

1.2. The third-party observation received on 14-11-2012 with letter of 02-11-2012 pursuant to Art. 115 EPC has been taken into account.

The third-party observation refers to the Traditional Knowledge Digital Library (TKDL) and it describes that Hypericum perforatum Linn., Neem, Quercus coccifera and Ruta graveolens Linn. have been used in the Indian systems of medicine since long, in the treatment of ulcers and for wound healing through local application.

This observation supports the information already anticipated, in documents D1-D5 and discussed in detail under paragraphs 4.1., 4.2. and 4.3. in the previous communication of the examining division, that the mentioned herbal extracts have a long tradition as antimicrobial agents.

2. Amendments, Article 123(2) EPC

2.1. The amendments filed with the letter dated 11-09-2013 do not introduce subject-matter which extends beyond the content of the application as filed, and therefore they comply with the requirements of Article 123(2) EPC.

3. Clarity, Article 84 EPC

3.1. The expression "Method according to anyone of the previous claims" in method claims 4, 5 and 6 also refers to products claims 1-3 rendering the category of said claims unclear. In order to comply with the requirements of Article 84 EPC, the applicant is suggested to reword such expression as "Method for the preparation of a substrate according to any of claims 1 to 3", which is in line with the expression used in method claims 9 and 11-13 as originally filed.

4. Inventive Step, Article 56 EPC

4.1. The examiner cannot agree with the arguments contained in the letter of the applicant dated 11-09-2013 for the following reasons.

4.2. Document D1 is considered as the closest prior art to the subject-matter of the present application. Document D1 discloses an adhesive composition of polymerizable 1,1-disubstituted ethylene monomer stabilized with an oil-soluble herbal extract such as St. Johns wort or quercetin (cf. claims 1-4), or neem extract (cf. claim 6). The dual function stabilizer in the polymer film described in D1 has stabilization effects to the composition with an enhanced and extended shelf-life and enhanced wound healing properties when utilized for medical purposes (cf. paragraphs 0016 and 0017). In D1, a polymerized film is made by polymerizing the 1,1-disubstituted ethylene monomer of the adhesive composition (cf. claims 1 and 64). The active principles in St. John's wort extract are hyperforin and hypericin and in neem oil is azadirachtin (see handbook D4 "Medical Plants of the World", van Wyk and Wink, pages 401 and 413).

4.3. The subject-matter of **independent claim 1** differs from D1 in the polymeric substrate itself, concretely in the selection of the polymeric materials and in its constitution in form of polymer fibers with a diameter lower than 1 µm.

The technical effect of such difference is not apparent from the present application for the following reasons. The experimental results provided in example 1 of the present application show that a poly(L-lactic acid) (PLLA) fibrous support loaded with either 25% or 50% (w/w) of undisclosed antimicrobial substances displayed an antibacterial activity in cultures of *S. aureus, P. aeruginosa and E. coli.* The further information given in example 1A of the annex to the applicant's letter dated 28-12-2012 indicates that a slightly larger extent of antibacterial activity may be associated with the PLLA substrate comprising fibers with a mean diameter value of 500 nm compared to those with a mean diameter value of 90000 nm even at a lower loading of antimicrobial substance. The examiner is of the opinion that the antimicrobial effect cannot be solely attributed to the diameter of the polymer fibers in the present application, but as well to the selected polymeric material in example 1A and to the particular antimicrobial substance/s used, even when the antimicrobial agent in 1A has not been disclosed. The number of alternative polymeric materials and the number of alternative antimicrobial substances falling within the scope of the present claim 1 is such that it is unlikely that all of them possess the type and level of activity required to achieve the antimicrobial effect essential for the resolution of the problem. Considerations regarding possible interactions between a certain polymeric material and a certain antimicrobial substance should also be taken into account. Therefore, it is not possible to extrapolate the modest improvement of the antibacterial activity found for the thinner PLLA fibers in example 1A of the annex to the letter of 28-12-2012 to all the polymeric materials and to all the antimicrobial substances listed in claim 1, nor to any combination thereof.

Besides, the following passage found in example 1A on page 4 of the annex to the letter of 28-12-2012 is confusing:

> "The scaffolds showed a remarkable decrease of cell viability in 24 hours (up to 60%), indicating a clear antibacterial activity. A film of PLLA containing 50wt % of antimicrobial substances prepared by solvent casting showed a decrease of cell viability in 24 hours lower compared to that of the corresponding scaffold 50 (30% vs 60%)".

On one side it is stated that the scaffolds in fibrous form reached a decrease of cell viability in 24 hours up to 60%, which is supported as well by the provided figures. Next, it is attributed to the corresponding PLLA casted film a lower decrease of cell viability in 24 hours than that of the fibrous scaffold 50, when actually the numbers indicate the contrary, being the aforementioned 60% cell viability of the fibrous scaffold 50 a weaker performance than the 30% cell viability of the casted film. Therefore, the provided information is contradictory and does not further contribute to the alleged technical effect.

Therefore, in view of D1, the objective technical problem underlying the present application can be considered as to provide an alternative composition for wound healing.

All the polymers listed in claim 1 are well-known substrate materials and are excipients used often in the field of wound healing formulations. The preparation of thin fibers thereof (obtainable by electrospinning) belongs to the common general knowledge in the preparation of substrates for application of remedies onto the skin. Besides, it is known from D1 that the polymerizable compositions may further contain a fibrous reinforcement such as PGA microfibrils (cf. paragraph 0061). In the absence of a technical effect, it would have been obvious for the skilled person starting from D1, to select any common polymeric fibrous material to arrive to the subject-matter of claim 1 of the present application. Consequently, the subject-matter of claim 1 does not involve an inventive step (Article 56 EPC).

4.4. The subject-matter of **dependent claim 2** additionally differs from D1 in that the composition contains a mixture of hyperforin and azadirachtin in the form of a mixture of hyperycum flowers or hypericum oleolite in neem oil.

The technical effect of such difference is not apparent from the present application.

The use of oil-soluble herbal extracts of the genus Hypericum (St. John's wort) or of the genus Azadirachta (neem) to promote wound healing and to stabilize an adhesive composition is known from D1 (cf. claims 4-6). Oleolite preparations of the aerial parts of the genus Hypericum have been used since ancient times as disinfectant to promote wound healing and belong to the common general knowledge in the field of ethnomedicine (see D4 page 175, D5 page 7 and third-party observation referring to the Traditional Knowledge Digital Library). In the absence of a particular technical effect, the mixture of hypericum flowers in neem oil comes with the customary practice of the skilled person in order to solve the problem posed. Consequently, the subject-matter of claim 2 does not involve an inventive step (Article 56 EPC).

4.5. The subject-matter of **dependent claim 3** additionally differs from D1 in that the polymeric material is mesh-grafted.

The technical effect of such difference is not apparent from the present application. The wound healing performance attributed in example 1A of the annex to the PLLA mesh-grafted scaffold compared to the not mesh-grafted one or to the PLLA film, cannot be acknowledged for all the polymeric materials and all the antimicrobial substances falling within the scope of claim 3, moreover when the antimicrobial substance appears absent or undisclosed in the mentioned example.

4.6. The subject-matter of **independent method claims 4, 5 and 6** differs from D1 in that the polymeric substrate is formed by electrospinning and in the loading of the antimicrobial substance.

The technical effect of such difference is not apparent from the present application.

Therefore, in view of D1, the objective technical problem underlying claims 4-6 can be considered as to provide an alternative method to prepare a composition for wound healing.

The use of electrospinning to draw fibers of a polymeric material belongs to the common general knowledge in the field of polymer sciences. The different ways to incorporate the antimicrobial substance are merely one of several straightforward possibilities which the skilled person would select, depending on the circumstances, without exercising inventive skill, in order to solve the problem posed. The composition in D1 is made of a polymerizable monomer (cf. claim1). The composition in D1 may contain materials such as a polymerization initiator or a cross-linking agent for initiating polymerization and/or cross-linking of the polymerizable monomer material (cf. paragraph 0064). It would have been obvious for the skilled person to polymerize the composition of D1 while using common means such as electrospinning to arrive to the subject-matter of claims 4-6 of the present application. Consequently, the subject-matter of claims 4-6 does not involve an inventive step (Article 56 EPC).

4.7. The previous reasoning applies *mutatis mutandis* to the "product for use" claims 7 and 8. Consequently, the subject-matter of claims 7 and 8 does not involve an inventive step (Article 56 EPC).

5. Further remarks

5.1. It is not at present apparent which part of the application could serve as a basis for a new, allowable claim. Should the applicant nevertheless regard some particular matter as patentable, the applicant is requested to file suitable amendments which take account of the above comments for the further prosecution of the application. If the amendment filed fails to overcome the objections raised above, it appears necessary to summon the applicant for oral proceedings.

5.2. In order to facilitate the examination of the conformity of the amended application with the requirements of Article 123(2) EPC, the applicant should clearly identify the amendments made, irrespective of whether they concern amendments by addition, replacement or deletion, and indicate the passages of the application as filed on which these amendments are based (see Guidelines H-III, 2.1).