NEW EMD FORMULATION COMPRISING PGA

![Figure 9](image)

**Abstract:** Enamel Matrix Derivative (EMD) proteins and enamel matrix proteins are widely used in clinical dentistry because of their ability to promote regeneration of soft and hard tissues and to reduce inflammation and infections. The present invention relates to the surprising finding that a pharmaceutical, dental and/or cosmetic formulation, which comprises purified Enamel Matrix Derivative (EMD) proteins and/or enamel matrix proteins and sterilized Propylene Glycol Alginate (PGA), wherein the sterilized PGA is obtained from non-sterilized PGA having a weight average molecular weight (Mₚ) of between 250-500 kDa, is more stable over time, especially, the pH is more stable over time.
before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K38/39 A61K47/36 A61Q11/00

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K A61Q

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, EMBASE, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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</table>

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"B" earlier document but published on or after the international filing date
"C" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"D" document referring to an oral disclosure, use, exhibition or other means
"E" document published prior to the international filing date but later than the priority date claimed
"F" 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
"G" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"H" 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.
"I" document member of the same patent family

Date of the actual completion of the international search: 18 January 2012

Date of mailing of the international search report: 07/05/2012

Name and mailing address of the ISA:
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016

Authorized officer: Escol ar Blasco, P
<table>
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<tr>
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<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
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</table>
**INTERNATIONAL SEARCH REPORT**

### Box No. II  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. **☐** Claims Nos.:
   - because they relate to subject matter not required to be searched by this Authority, namely:

2. **☐** Claims Nos.:
   - because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. **☐** Claims Nos.:
   - because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box No. III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

- see additional sheet

1. **☐** As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. **☐** As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. **☐** As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. **☒** No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

   - 1-5, 8-II (completely); 6, 7, 15-28, 36-38(partly)

**Remark on Protest**

- **☐** The additional search fees were accompanied by the applicant’s protest and, where applicable, the payment of a protest fee.

- **☐** The additional search fees were accompanied by the applicant’s protest but the applicable protest fee was not paid within the time limit specified in the invitation.

- **☒** No protest accompanied the payment of additional search fees.

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Form PCT/ISA/21 0 (continuation of first sheet (2)) (April 2005)
This International Search Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-5, 8-II (completely) ; 6, 7, 15-28, 36-38 (partially)

   A pharmaceutically, dental and/or cosmetic composition comprising enamel matrix x proteins or derivatives (EMD) and using weight/vol % sterilized propylene glycol alginate (PGA) of an average molecular weight above 130 kDa, and uses thereof.

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2. claims: 12-14, 29, 30 (completely); 6, 7, 15-28, 38 (partially)

   A pharmaceutically, dental and/or cosmetic composition comprising enamel matrix x proteins or derivatives (EMD) and propylene glycol alginate (PGA) obtained from e-beam sterilized PGA of an average molecular weight of at least 250 kDa; uses thereof and process of producing it.

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3. claims: 31, 32 (completely); 36-38 (partially)

   Use of an e-beam sterilized PGA with an average molecular weight before sterilization of 250-500 kDa for manufacturing a pharmaceutically, dental or cosmetic composition comprising enamel matrix x proteins or EMD and e-beam sterilized PGA of molecular weight above 130 kDa, wherein said composition has a pH value above 3.5 over a period of at least 18 months.

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4. claims: 33-35

   A method for determining the maximal concentration of sterilized PGA in order to obtain the desired stability of a PGA, characterized in that said method comprises the following steps: a) measuring the initial pH of a sterilized PGA; b) deciding the durability period of the composition; using the obtained results from a) and b) in the following equation:

   \[ \text{pH} \times 3.5 = \text{pHO} - 3.5 / 0.0205 \times [\text{sterilizedPGA}] - 0.0914 \]

   wherein \( \text{pH} 3.5 \) is the durability period and \([\text{sterilizedPGA}]\) is the applied sterilized PGA concentration.

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<table>
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<tr>
<th>Patent document cited in search report</th>
<th>Publication date</th>
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<td>EP 1862170</td>
<td>A1</td>
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