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Search Report Sample

Date: Nov. 9th, 2007

To:
XXXXXXX

JAPANESE PRIOR ART SEARCH REPORT
INVALIDATION SEARCH

This is to summarize our Japanese prior art search results for target XXXXX, titled "XXXXXX".

Search language:
Japanese

Period of the search:
Before July 31st, 1992 (claimed priority date of the target patent)

Database used in the search:
NRI, Patolis and IPDL

Japanese patent type searched:
Japanese patent documents, both unexamined and examined

SEARCH RESULTS
We used NRI, PATOLIS and IPDL to conduct 2 searches for Japanese patent documents, both unexamined and examined. Full text search and combination of Japanese F term, FI code (Japanese patent classifications), and IPC are used. 335 hits are picked up in the searches. After reviewing these 335 hits, 6 Japanese patent documents that are considered to be documents of relevancy or general state of the art are uncovered. These 6 Japanese patent documents are summarized below.

Table 1 Documents Considered to be Relevant or General State of the Art:

No.	Patent No.	Title	Relevance to the target patent*
1	JP61-126014	Aqueous Liquid Drug for Transnasal Administration	A
2	JP01-308235	Human Growth Hormone for Transnasal Administration	Y
3	JP01-151525	Composition Containing Physiologically Active Polypeptides	A
4	JP02-115118	Injection	A
5	JP62-126135	GRF Preparation for Administration Through Nose	A
6	JP03-83931	Low-Irritation GRF Preparation for transnasal Administration	Y

*Note:
X: document of particular relevance: the claimed invention cannot be considered novel or non-obviousness when the document is taken alone.
Y: document of relevance: the claimed invention cannot be considered non-obviousness when the document is combined with one or more other documents, such combination being obvious to a person skilled in the art.
A: general state of the art: not considered to be of particular relevance.
P: documents published prior to the filing date of the target patent but later than the claimed priority date.

Please note that the relevance ranking above is based on our searcher and reviewer's non-patent-attorney opinion, and it may change significantly depending on many circumstances.

Titles, Abstracts of the Japanese Patent Documents:

Titles, abstracts, main claim translation, and other bibliographical information of the 6 patent documents are summarized below.

Please note that the abstracts are obtained from JPO and there are flaws in the translation.

1. Publication number: JP61-126014

Publication date: 1986-06-13
Inventor: Sekine Kunio; Suzuki Yoshiki; Yamashita Gentaro; Nagai Tsuneji
Applicant: Teijin Ltd
Title: Aqueous Liquid Drug for Transnasal Administration

Abstract:

Purpose: To provide a liquid agent having a specific viscosity, containing a physiologically active polypeptide and hydroxypropylcellulose in an aqueous base, and capable of effectively transferring the polypeptide through the nasal mucosa to the body.
Constitution: The titled liquid agent having a viscosity of 2-4,000cp (preferably 5-1,000cp) at 25 deg.C and a pH of 3.5-7.5 (preferably 5.0-7.5) is produced by dissolving (A) a physiologically active polypeptide and (B) a hydroxypropylcellulose in an aqueous base. The component A is preferably a peptide hormone having a molecular weight of 300-300,000 (e.g. calcitonin, insulin, lutenizing hormone, etc.), physiologically active protein, vaccine, etc., and the aqueous base is water, physiological saline water, buffer solution, etc. The active substance can be absorbed in high efficiency without causing pain, by administering the above liquid agent to the nasal cavity.

Family list
3 family member for JP61-126014 derived from 1 application
Publication info: JP1679325C
JP3038255B
JP61-126014 A

Main claim translation:

Claim 1: An aqueous preparation for transnasal administration, comprising a physiologically active polypeptide and hydroxypropylcellulose in an aqueous base adapted to application to nasal mucosa, said aqueous preparation has a viscosity at the range of 2-4000cP at 25 C◦

Comments from the searcher/reviewer:
This patent application discloses an aqueous preparation for nasal administration that comprises polypeptides having physiological activity and hydroxypropy-cellulose. The polypeptides having physiological activity is selected from calcitonin, insulin, growth hormone, etc. (page 2, right column, in the Japanese pdf file). pH of the aqueous preparations is 3.5-7.5, preferably 5.0-7.5 (page 3, left column).

2. **Publication number: JP01-308235**
Publication date: 1989-12-12
Inventor: Kagaya Seiya; Inaba Noriko; Sonobe Takashi
Applicant: Yamanouchi Pharma Co Ltd
Title: Human Growth Hormone for Transnasal Administration

Abstract:
Purpose: To obtain the subject agent for nasal administration free from action to damage the tissue such as nasal mucosa, by compounding o-acylcarnitine as an absorbefacient.
Constitution: A human growth hormone (somatotropin) and a compound of formula (R is 2-20C acyl) or its salt are included in a liquid diluent or carrier suitable for the application to nasal mucosa. The compound of formula is preferably a 8-18C compound, especially o-octanoylcarnitine, o-lauroylcarnitine or o-palmitoylcarnitine and the weight ratio of the compound to the human growth hormone is 1:0.007-2.3, preferably 1:0.07-0.8 when the composition is liquid and is 0.007-150, preferably 1:0.07-50 when the composition is solid or semi-solid.

Main claim translation:
Claim 1: A medicinal preparation for transnasal administration of human growth hormone, comprising human growth hormone and o-asylcarnitine or its salt contained in a liquid diluent or carrier adapted for application to nasal mucosa.

Comments from the searcher/reviewer:
This patent application discloses a medicinal preparation of human growth hormone for transnasal administration. The preparation comprises human growth hormone and o-asylcarnitine or its salt. The preparation can be an aqueous solution, hydrogel or solid powder. The aqueous solution has a pH of 5.5-8.5 (page 2, left column in the original Japanese pdf file). o-asylcarnitine or its salt is added as an absorption accelerator. Non-ionic surfactants and preservatives can also be added in the aqueous solution.

3. **Publication number: JP01-151525**
Publication date: 1989-06-14
Inventor: Miura Ikufumi; Kotani Kikuo
Applicant: Toyo Jozo Kk
Title: Composition Containing Physiologically Active Polypeptides

Abstract:
Purpose: To provide the title composition containing physiologically active polypeptides and lecithin hydroxide and effective in preventing the adsorption of

physiologically active polypeptides to a tool or vessel, etc.
Constitution: The objective composition contains (A) physiologically active polypeptides such as calcitonin, ACTH, PTH, insulin or growth hormone and (B) a lecithin hydroxide preferably having a hydroxyl value of 150-400. The lecithin hydroxide can be produced by hydroxylating a part or total of unsaturated bond existing in the fatty acid segment of lecithin and has high hydrophilic property and excellent stability compared with lecithin. The amount of the hydroxide is 0.0005-1.0% in the composition having the form of an aqueous solution or aqueous suspension. Both components of the above composition may be present in the same aqueous solution, aqueous dispersion or a solid or may be prepared as separate dry solid materials and mixing the solid at the same time.

Main claim translation:
Claim 1: A composition comprising a physiologically active polypeptide and hydroxylated lecithin.
Claim 2: The composition according to claim 1, wherein the physiologically active polypeptide is selected from calcitonin, ACTH, PTH, insulin, secretin, oxytocin, growth hormone, angiotensin, bradykinin, ß-endorphin, glucagon, and dynorphin.

Comments from the searcher/reviewer:
This patent application discloses a composition containing a physiologically active polypeptide and hydroxylated lecithin. The polypeptide is selected from insulin, growth hormone, etc. The composition can be in the form of aqueous solution, aqueous suspension solution or freeze-dried powder.

4. **Publication number: JP02-115118**
Publication date: 1990-04-27
Inventor: Yada Noboru; Murakami Teruo; Amagase Harunobu
Applicant: Wakunaga Pharma Co Ltd
Title: Injection

Abstract:
Purpose: To obtain an injection, containing a fatty acid derivative as at least one of adjuvant ingredients, capable of improving migration properties of a main drug into blood and having treating effects.
Constitution: The objective substance obtained by containing peptides, etc., as a main drug and a fatty acid derivative (e.g., polyoxyethylene sorbitan ester of a fatty acid) as an adjuvant ingredient, as necessary, blending other normally used recipients, dissolution adjuvants, stabilizers, preservatives, suspending agents, emulsifying agents, etc., therewith and preparing a pharmaceutical as an injection according to a conventional method. The amount of the blended fatty acid derivative as the adjuvant ingredient is normally 0.01-10% (wt./vol.), preferably 0.1-2% (wt./vol.) based on the solution to be administered depending on the kind of the main drug and purpose of treatment.

Main claim translation:
Claim 1: An injectable solution consisting of a fatty acid derivative as at least one of the supplementary additives

Comments from the searcher/reviewer:
This patent application teaches an injectable solution having a fatty acid derivative as one of the supplemental additives. The primary component of the injectable

solution is a polypeptide selected from growth hormone, calcitonin, secretin, etc. (page 2, right column in the original Japanese pdf file). Both aqueous solution and freeze-dried powder are disclosed in embodiment portion using human Epidermal Growth Factor (hEGF) as the example.

5. **Publication number: JP62-126135**
Publication date: 1987-06-08
Inventor: Fujioka Takaharu; Takada Yoshihiro; Osada Akihiko; Tsuda Masabumi
Applicant: Sumitomo Pharma
Title: GRF Preparation For Administration Through Nose

Abstract:
Purpose: The titled preparation containing a surface active agent having a steroid skeleton or triterpene skeleton.
Constitution: A GRF preparation for administration through the nose comprising a Growth Hormone Releasing Factor (GRF: peptide showing GH releasing activity) and 0.01-50w/v%, more preferably 0.01-30w/v% in aqueous solution or suspension of one or a combination of surface active agents (e.g., saponin, salt of bile acid, squalene, etc.,) containing a steroid skeleton or triterpene skeleton and, if necessary, a buffer solution, stabilizer, preservative, dissolution auxiliary, pH adjustor, isotonic agent, etc. Administration through the nose means absorption of drug from mucosa of nasal cavity, a solution which can be sprayed into the nasal cavity is convenient or the preparation may be processed into lyophilized powder with respect to shelf stability and made into a solution in use. The pH of the preparation is preferably 2-7 with respect to stability.

Main claim translation:
Claim 1: A GRF preparation for transnasal administration, consisting of a surfactant having steroid skeleton or triterpene skeleton.
Claim 2: The GRF preparation for transnasal administration according to claim 1, wherein the surfactant is saponin or bile salt.

Comments from the searcher/reviewer:
This patent application discloses a growth hormone releasing factor (GRF) preparation for transnasal administration. The GRF preparation for transnasal administration consists of a surfactant with steroid skeleton or triterpene skeleton. The preparation can be aqueous solution, suspension, gel or freeze-dried powder, The pH of the preparation is preferably 2 - 7.

6. **Publication number: JP03-83931**
Publication date: 1991-04-09
Inventor: Fujioka Takaharu; Takada Yoshihiro; Aisaka Ayumi
Applicant: Sumitomo Pharma
Title: Low-Irritating GRF Preparation for transnasal Administration

Abstract:
Purpose: To obtain the subject pharmaceutical, containing sodium chloride and/or sugar alcohol as an additive, capable of exhibiting growth hormone releasing activity in living bodies and relieving nasal mucosal irritancy of a peptide useful in clinical

medicine and usable for a long period without any toxic reaction.
Constitution: A pharmaceutical containing sodium chloride and/or sugar alcohol as an additive. In use, the pharmaceutical is formed into a solution so as to enable spraying or dripping of a peptide which is an active ingredient into the nasal cavity or freeze-dried pharmaceutical from aspects of preservation stability, dissolved in a dissolving solution and employed in use. The content of the active ingredient in the pharmaceutical is normally 0.001-10wt./vol.% in an aqueous solution or suspension. Mannitol, sorbitol, etc., are cited as the sugar alcohol employed as the aforementioned additive. The amount thereof used is 0.1-30wt./vol.% in the case of the aqueous solution or suspension and the amount of the sodium chloride used is 0.01-10wt./vol.%.

Family list
3 family members for JP03-083931 derived from 3 applications
Publication info: CA2024171
EP0417930 A1
JP03-083931 A

Main claim translation:
Claim 1: A low-irritation GRF preparation for transnasal administration, consisting of sodium chloride and /or a sugar alcohol as the additives.
Claim 2: The low-irritation GRF preparation for transnasal administration according to claim 1, wherein the sugar alcohol additive is mannitol or sorbitol.

Comments from the searcher/reviewer:
The patent application teaches a low-irritation GRF (growth hormone release factor) nasal preparation having sodium chloride and sugar alcohol as the additives. The sugar alcohol is mannitol or sorbitol. GRF is a peptide that has the activity of growth hormone.

SUMMARY AND COMMENTS:

We got about 335 hits in the search using full text search and combination of Japanese F term, FI code (Japanese patent classifications), and IPC. List of the hits reviewed is attached for your reference. After reviewing these hits, 6 Japanese patent documents that are considered to be documents of relevance or general state of the art are cited in this report for your reference. Machine translation output of the 6 Japanese patent documents are also provided for your convenience.

Please note that the relevancy ranking in Table 1 is based on our non-patent-attorney opinion, so we strongly recommend you to have a more comprehensive review for the Japanese patent documents provided.

Would you please review the search report and the attachments. If you have any questions regarding the search results, or if there is anything else we can be of your assistance, such as human translation for the cited Japanese patent applications, please do not hesitate to contact us.

Sincerely yours,

Search: XXX
Review and machine translation: XXX, XXX

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Attachment:

- Japanese patent documents cited in this report (6 pdf files)
- Machine translation output (6 word files)
- List of the hits reviewed from the searches (excel file)