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24/8/99.

RP-HPLC (10-50% acetonitrile gradient over 40 min, flow rate 1.2ml/minute) retention time = 27.7 minutes; mass spectrometry, m/e (ES+) 1021.6 $(MH)^+$; amino acid analysis gave Thr 0.61, Ala 3.80, Arg 1.22, IIb 0.97;

Phv-Arg-Ala-Ala-Ala-Thr-IIb-Ala-Papa-OH (SEQ ID NO: 34) (155mg);
RP-HPLC (10-50% acetonitrile gradient over 40 min, flow rate 1.2ml/minute) retention time = 24.2 minutes; mass spectrometry, m/e (ES+) 1007.5 $(MH)^+$; amino acid analysis gave Thr 0.62, Ala 3.78, Arg 1.20, IIb 0.98.

Example 34.

Phv-Arg-Ala-Ala-Ala-Thr-IIb-Ala-Papa-N$(CH_2CH_2)_2$N-$(CH_2)_2$O$(CH_2)_2$OH
(SEQ ID NO: 35)

4-[2-(2-hydroxyethoxy)ethyl]piperazine (235 mg) was added to a mixture of Phv-Arg-Ala-Ala-Ala-Thr-IIb-Ala-Papa-OH (135mg), HBTU (51 mg), DIPEA (47 microlitres) and DMF (10 ml) and the mixture was stirred for 60 minutes. Volatile material was removed by evaporation, and the residue was purified by preparative HPLC, using a similar procedure to the described in Example 1.4, to give Phv-Arg-Ala-Ala-Ala-Thr-IIb-Ala-Papa-N$(CH_2CH_2)_2NCH_2CH_2$- OCH_2CH_2OH (SEQ ID NO: 35)(115mg). The peptide was characterised by HPLC, mass spectrometry and amino acid analysis in a similar manner to that described for Example 1.4; RP-HPLC (eluting with acetonitrile and water containing 0.1%TFA, using a 10-50% acetonitrile gradient over 40 minutes, flow rate 1.2ml/minute) retention time = 18.83 minutes; mass spectrometry, m/e (ES+) 1163.8 $(MH)^+$; amino acid analysis gave Thr 0.62, Ala 3.80, Arg 1.22, IIb 0.97.

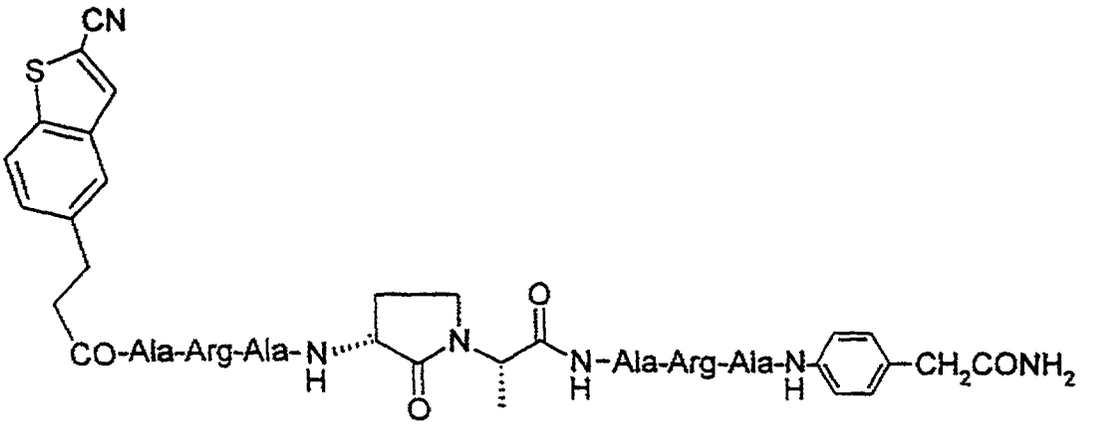
Example 35

The compounds of the invention may be administered for therapeutic or prophylactic use to warm-blooded animals such as man in the form of conventional pharmaceutical compositions, a typical example of which includes the following:-

Injectable Solution

0.01 to 100 mg of active ingredient is dissolved in up to 2 ml of an aqueous injection vehicle to give a concentration of active ingredient between 0.01 to 100 mg/ml. The aqueous

and



or a pharmaceutically acceptable salt thereof, in which Phv represents a 5-phenylvaleryl group.

11. A pharmaceutical composition which comprises a peptide derivative of the formula I, or a pharmaceutically acceptable salt thereof, in association with a pharmaceutically acceptable diluent or carrier.

12. A process for the manufacture of a peptide derivative, or a pharmaceutically acceptable salt thereof, as claimed in claim 1, comprising sequentially coupling in the appropriate order suitably protected amino acids or sequences of two or more suitably protected amino acids, a suitably protected group of the formula H-II-OH or H-III-OH and optionally a suitably protected group of the formula R^4-H, followed by optional functional group modification of the N-terminal amino group, to introduce a hydrophobic group P, and removal of any remaining protecting groups and any solid support.

13. The use of a peptide derivative of formula I as claimed in claim 1, or a pharmaceutically acceptable salt thereof, in the production of a novel medicament for use in the treatment of a MHC class II dependent T-cell mediated autoimmune or inflammatory disease.

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14. The use of a peptide derivative of formula I as claimed in claim 1, or a pharmaceutically acceptable salt thereof, in the production of a novel medicament for use in the treatment of rheumatoid arthritis or multiple sclerosis.

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(54) Title: PEPTIDE DERIVATIVES

(57) Abstract

The invention concerns pharmaceutically useful peptide derivatives of the formula (I): P-R^1-R^2-R^3-R^4, in which P, R^1, R^2, R^3, and R^4 have the various meanings defined herein, and their pharmaceutically acceptable salts, and pharmaceutical compositions containing them. The novel peptide derivatives are of value in treating MHC class II dependent T-cell mediated autoimmune or inflammatory diseases, such as rheumatoid arthritis. The invention further concerns processes for the manufacture of the novel peptide derivatives and the use of the compounds in medical treatment.