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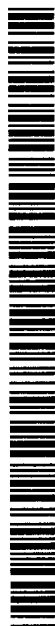
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(54) Title: **CICLESONIDE-CONTAINING AQUEOUS PHARMACEUTICAL COMPOSITION**

(57) Abstract: The present invention provides an aqueous pharmaceutical composition containing ciclesonide and hydroxypropylmethylcellulose, wherein the ciclesonide is dispersed in an aqueous medium in the form of solid particles. The composition is able to avoid variations in the concentrations of ciclesonide during production as well as avoid decreases in the recovery rate of ciclesonide

DESCRIPTION

CICLESONIDE-CONTAINING AQUEOUS PHARMACEUTICAL COMPOSITION

Field of Invention

5 The present invention relates to a ciclesonide-
containing aqueous pharmaceutical composition for use in
drug therapy that contains ciclesonide and
hydroxypropylmethylcellulose, wherein said ciclesonide is
dispersed in an aqueous medium in the form of solid
10 particles. More particularly, the present invention
relates to a ciclesonide-containing aqueous
pharmaceutical composition having excellent ciclesonide
dispersivity during production as compared with
conventional aqueous pharmaceutical compositions.

15 Background Art

Ciclesonide aqueous pharmaceutical compositions
containing ciclesonide dispersed in an aqueous medium in
a form of solid particles are expected to represent a
useful drug form for reasons that include 1) it is not
20 necessary to completely dissolve ciclesonide, 2) it can
be directly administered to an affected site by spraying
and so forth for treatment of local diseases such as
those of the nasal mucosa, eyes and epidermis, and 3)
they are easier to swallow than tablets or granule and so
25 forth.

When present in an aqueous medium, ciclesonide is
resistant to wetting and easily aggregates. The addition
of wetting agent such as Polysorbate 80 and powerful
stirring and so forth during production have been used in
30 the prior art for the purpose of dispersing drug having
such properties in an aqueous medium in a stable state.

Improvement of drug dispersivity of aqueous
pharmaceutical compositions containing a drug dispersed
in an aqueous medium in form of solid particles by
35 addition of cellulose-based polymer is disclosed in
Morishima et al. patent specification of W099-37286.
However, this patent relates to the redispersion of a

drug that has settled during storage, and is
fundamentally different from the present invention which
relates to overcoming drawbacks of the migration of
ciclesonide towards bubbles formed by powerful stirring
5 during the production, and the adsorption of ciclesonide
to the walls of the production apparatus. Moreover, the
concentration of the cellulose-based polymer in the
patent specification of Morishima et al. is 0.0001 to
0.003%, and methylcellulose can be used in place of
10 hydroxypropylmethylcellulose for the cellulose-based
polymer, while the addition of a nonionic surfactant is
also required. It is not easy to deduce the present
invention from this patent in which the optimum value of
the hydroxypropylmethylcellulose concentration is from
15 0.01% w/w to 0.5% w/w, and does not require a surfactant.

Disclosure of the Invention

During the course of production of ciclesonide
aqueous pharmaceutical compositions, high shearing force
is required to disperse ciclesonide and it is necessary
20 to powerfully stir ciclesonide-containing aqueous
pharmaceutical composition. Ciclesonide migrates to the
bubbles formed at this time. Since this results in an
increased concentration of ciclesonide in the upper
portion of the ciclesonide aqueous pharmaceutical
25 composition being higher than that in the lower portion,
variation occurs in the ciclesonide concentration of
ciclesonide aqueous pharmaceutical compositions produced.
Moreover, the recovery rate decreases due to adsorption
of ciclesonide to the walls and so forth of the
30 production apparatus.

These variations in ciclesonide concentration and
adsorption of ciclesonide to the production apparatus
were hardly improved at all by the addition of wetting
agents such as Polysorbate 80 that have been used in the
35 prior art. Conversely, the amount of formed bubbles
increases resulting in promotion of further variation in
ciclesonide concentration.

Therefore, there is a considerable need for the development of a ciclesonide aqueous pharmaceutical composition that is able to avoid variations in ciclesonide concentrations during production as well as the decrease in ciclesonide recovery rate.

Namely, the object of the present invention is to provide a ciclesonide aqueous pharmaceutical composition that avoids variations in ciclesonide concentration during production as well as decreases in the ciclesonide recovery rate.

As a result of earnest studies to solve the above problems, the inventors of the present invention found that a ciclesonide aqueous pharmaceutical composition can be provided that avoids variations in ciclesonide concentrations during production as well as decreases in the ciclesonide recovery rate, by using a ciclesonide aqueous pharmaceutical composition containing ciclesonide and hydroxypropylmethylcellulose, thereby leading to completion of the present invention.

Namely, the present invention relates to an aqueous pharmaceutical composition containing ciclesonide and hydroxypropylmethylcellulose, wherein said ciclesonide is dispersed in an aqueous medium in form of solid particles.

Embodiment for Carrying Out the Invention

It is essential that composition of the present invention contain ciclesonide, while water-soluble, water-low soluble or water-insoluble drugs other than ciclesonide can be added. Specific examples of these include vasoconstrictors, bronchodilators, anti-allergic agents and expectorants.

Although the ciclesonide particles that can be used in the present invention may be of any size, they are preferably within the range of 10 nm to 100 μm , and particularly preferably within the range of 10 nm to 10 μm .

Although any substances may be used for the water-insoluble or water-low soluble substance that can be used in the present invention, a preferable example is a cellulose, and a particularly preferable example is crystalline cellulose.

In the present invention, the concentration of water-insoluble substance and/or water-low soluble substance present in form of solid particles in an aqueous medium is preferably 0.3% w/w and above, and particularly preferably 1% w/w to 10% w/w, relative to the total amount of the composition.

In addition, an aqueous polymer substance can also be added in the present pharmaceutical composition. Specific examples of such include propylene glycol alginate, pectin, low methoxyl pectin, gua gum, gum arabic, carrageenan, methylcellulose, carboxymethylcellulose sodium, xanthan gum and hydroxypropylcellulose, while particularly preferable examples include carboxymethylcellulose sodium, polyethylene glycol and hydroxypropylcellulose. In addition, crystalline cellulose carmellose sodium, is an example of a combination of these water-soluble substances and water-insoluble substances that can be used in the present invention, and it consists of a mixture of carboxymethylcellulose sodium and crystalline cellulose. Furthermore, in the case of adding these water-soluble polymer substances, the concentration of said substance is preferably 1% w/w to 30% w/w relative to the water-insoluble substance and/or water-low soluble substance.

The ciclesonide-containing aqueous pharmaceutical composition of the present invention is also required to contain hydroxypropylmethylcellulose. Although this may be of any grade, a specific example is hydroxypropylmethylcellulose 2910.

Although said hydroxypropylmethylcellulose may be present at any concentration, its concentration is

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