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(54) Title: ANORECTIC

(57) Abstract: The present invention relates to an anorectic containing a compound having a DGAT inhibitory activity (DGAT1 inhibitory activity) or a prodrug thereof or a pharmaceutically acceptable salt thereof as an active ingredient. The present invention provides an anti-obesity drug which is an anorectic that does not directly act on the central nervous system and is satisfactory in terms of activity, and a therapeutic strategy for preventing or treating obesity.

Description

ANORECTIC

Technical Field

The present invention relates to an anorectic action of a compound having a DGAT (diacylglycerol acyltransferase) inhibitory activity (e.g., DGAT1 inhibitory activity). Moreover, the present invention relates to a combined use of such DGAT inhibitors (e.g., DGAT1 inhibitor) and various drugs.

Background Art

It is known that various intracerebral neural activities and neurotransmitters are involved in the control of appetite in human and animals. These neural activities are affected by biochemical, neurological or endocrine signals that occur in the process of nutritive digestion, absorption, metabolism and storage.

Sugars and lipids themselves as nutrients, or metabolites in fat, muscule and liver cause biochemical signals that act promotively or suppressively on cerebral nerve activities involved in appetite.

It is also known that endocrine signals (e.g., CCK, GLP1, Enterostatin, ApoAIV etc.) or neural signals via chemical receptors of the gastrointestinal tract or from enteric plexus, during the process of digestion and absorption of sugars and lipids, affect gastrointestinal functions and cerebral nerve activities.

Moreover, it is known that fat tissue, which is a fat storage organ, produces endocrine or biochemical signals, such as leptin, adiponectin and free fatty acid, along with storage and consumption of fat. These signals alone or cooperative combinations of signals are considered to affect the central nervous system which controls appetite.

The DGAT1 inhibitor is expected to inhibit absorption of fat by suppressing re-synthesis of triglyceride in the

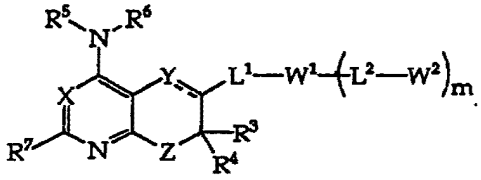
gastrointestinal tract, and changes the above-mentioned signals that affect function of the gastrointestinal tract or brain.

In addition, the DGAT1 inhibitor is expected to change biochemical or endocrine signals from fat tissue by suppressing re-synthesis of triglyceride in the fat tissue.

Furthermore, it has been reported that DGAT1 deficient mice show an accelerated sensitivity of brain function to leptin which is an anti-obese factor derived from fat tissue. Therefore, a similar effect is expected by the administration of a DGAT1 inhibitor.

In the meantime, as a compound having a DGAT inhibitory activity, the following compounds are known.

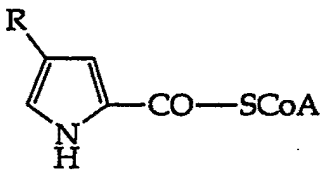
The following compound has been disclosed to have a DGAT inhibitory activity (e.g., WO2004/47755, published after the priority date of the present application).



(1)

This reference discloses inhibition of DGAT. However, disclosure of anorectic action resulting from the inhibition of DGAT as in the present application is not contained at all.

For example, the following compound has been disclosed to have a DGAT inhibitory activity (e.g., JP-A-H5-213985).

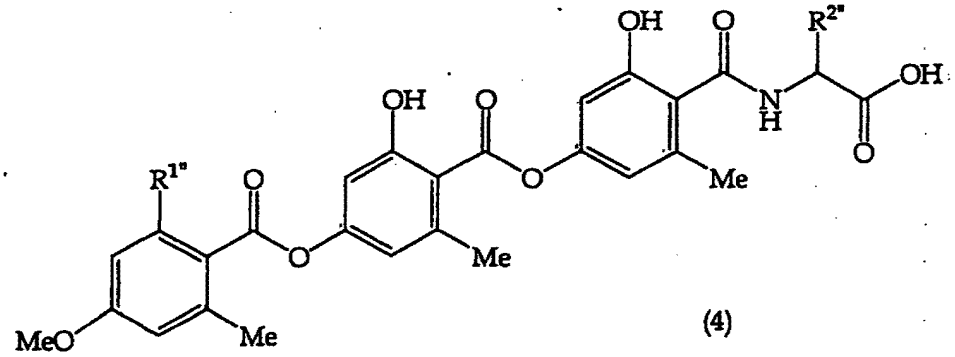


(3)

This reference discloses inhibition of ACAT and DGAT. However, disclosure of anorectic action resulting from the inhibition of DGAT as in the present application is not

contained at all.

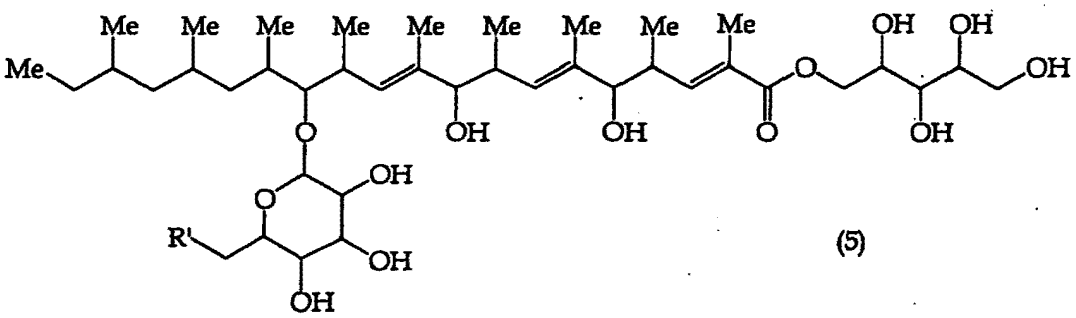
Similarly, the following compound has been disclosed to have a DGAT inhibitory activity (e.g., JP-A-H8-182496).



(4)

This reference discloses inhibition of DGAT. However, disclosure of anorectic action resulting from the inhibition of DGAT as in the present application is not contained at all.

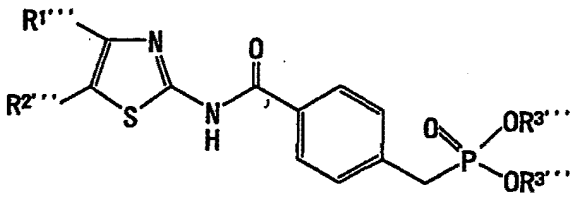
Moreover, the following compound has been disclosed to have a DGAT inhibitory activity (e.g., WO00/58491).



(5)

This reference discloses inhibition of DGAT. However, disclosure of anorectic action resulting from the inhibition of DGAT as in the present application is not contained at all.

Moreover, the following compound has been disclosed to have a DGAT inhibitory activity (e.g., JP-A-2004-67635).

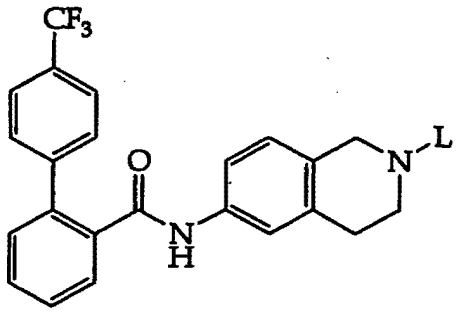


(6)

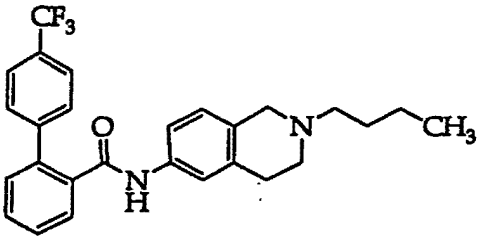
This reference discloses inhibition of DGAT. However,

disclosure of anorectic action resulting from the inhibition of DGAT as in the present application is not contained at all.

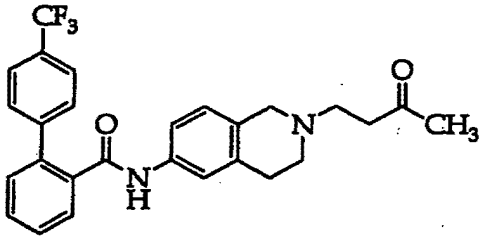
As a compound having an anorectic action, ApoB secretion/MTP (Microsomal Triglyceride Transfer Protein) inhibitors have been disclosed (e.g., JP-A-2001-181209). As such compound, for example, the following formula has been disclosed.



Specifically, the following compounds have been disclosed.



and



However, this reference does not disclose that these compounds have a DGAT inhibitory activity.

In addition, the reference discloses that similar compounds have been disclosed to have a suppressive action on fat absorption from small intestine, but does not disclose that these compounds have a DGAT inhibitory activity (e.g., JP-A-2001-172180).

While the development of anti-obesity drugs is currently ongoing, they are not satisfactory in terms of activity. The development of anorectic agents to prevent or treat obesity is also ongoing. However, since most of these anorectic agents directly act on the central nervous

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