Stable NOHA derivatives

General information

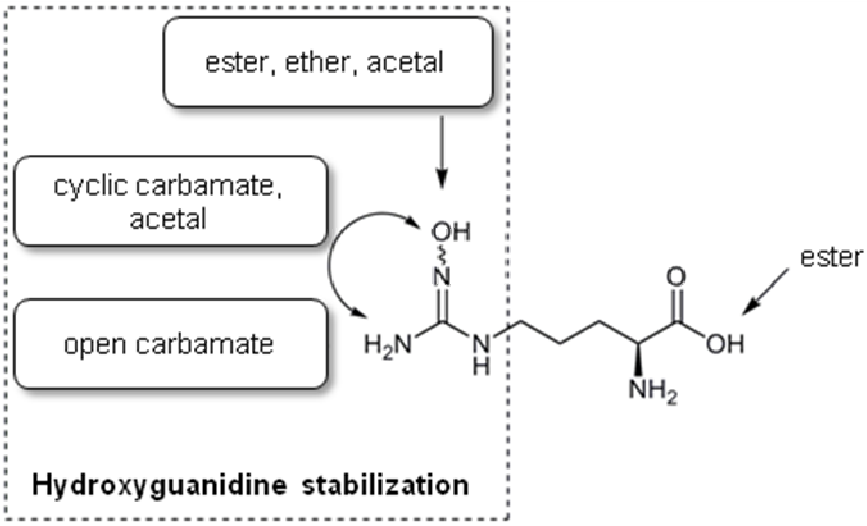
Nitric oxide (NO) is formed endogenously during a two-step oxidation from L-arginine via the intermediate NOHA (N^{ω}-hydroxy-L-arginine).

NO is a physiological mediator with versatile functions, such as the maintenance of vascular homoeostasis, neuronal signaling and inhibition of tumor cell growth. Furthermore, it prevents atherosclerotic events and serves as a cytotoxic agent in immune defense. An impaired NO availability results in hypertonia and cardiovascular and erectile dysfunction. On the other hand, NO overproduction can lead to a number of severe diseases as well, e.g. migraine, septic shock and ischemia. Thus a balanced regulation of NO formation is vital.

State of the art

The use of NOHA in its duality of actions (arginase inhibitor and NO precursor) enables such a balanced regulation and has been described and patented for a number of medical indications. However, in practice such a use is limited due to NOHA's disadvantageous pharmacokinetic profile which results mainly from the presence of an unsubstituted N-hydroxyguanidine function.

The invention



The substitution of the N-hydroxyguanidine function as depicted above leads to thermo- and oxidation-stable NOHA derivates, whose favorable characteristics make them the choice alternative to NOHA for therapeutic uses.

Utilisation concept

Licensing/selling of this invention is sought to a company that will produce, bring to market and distribute the described NOHA derivates. If desired PVA SH GmbH will further assist by arranging contact with the inventors.

Contact

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