NITRIC-OXIDE DONATING ANTI-INFLAMMATORY DRUGS: A NEW CLASS OF EFFECTIVE AND SAFE AGENTS

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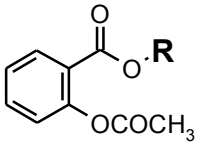
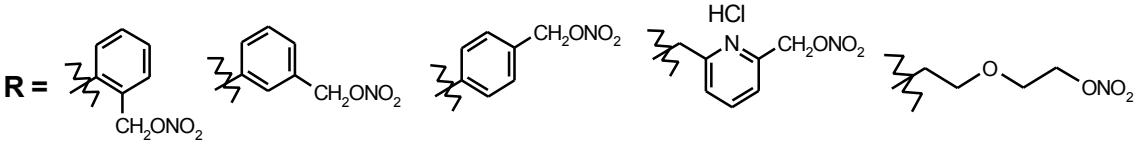
A new family of anti-inflammatory drugs capable of releasing nitric oxide (NO) has been synthesized. The rationale of this approach is based upon the pharmacological properties of NO, that is released in limited amount through the activity of esterases present in biological tissues (1,2). A common chemical feature of such drugs is the link of an established and effective moiety (*e.g.*, acetylsalycilic acid, flurbiprofen, prednisolone) with nitrate through a spacer (see figure). The chemical properties of the spacer, being alkyl or aryl, confer different pharmacological and pharmacokinetic action to the new chemical entity. Here we report the examples of some new derivatives of aspirin.





The intense efforts made to develop this concept has led to discovery and early development of innovative drugs which are now being investigated in clinical studies to assess their clinical usefulness (3,4, 5).

References

1. Del Soldato P. et al., *Trends Pharmacol. Sciences*, 1999, 20, 319-323.
2. Carini M. et al., *J. Pharmaceut. Biom. Anal.*, 2001, 26, 509-518.
3. Rossoni G. et al., *J. Pharm. Exp. Ther.*, 2001, 297, 380-387.
4. Napoli C. et al., *PNAS*, 2002, 99, 1689-1694.
5. Paul-Clark et al., *PNAS*, 2002, 99, 1677-1682