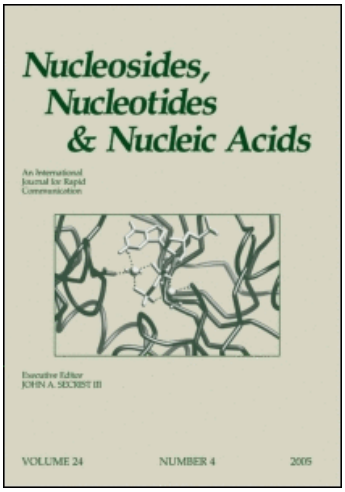


**Nucleosides, Nucleotides and Nucleic Acids**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

# Therapeutic Implications of The Unusually Long Half-Life of (E)-5-(2-bromovinyl)uracil (Bvura) In Vivo

C. Desgranges[a]; G. Razaka[b]; E. De Clercq[b]; H. Bricaud[b]
[a] Unité 8 de 1'INSERM, Pessac, France [b] Rega Institute, Katholieke Universiteit Leuven, Leuven, Belgium

**To cite this Article** Desgranges, C. , Razaka, G. , De Clercq, E. and Bricaud, H.(1985) 'Therapeutic Implications of The Unusually Long Half-Life of (E)-5-(2-bromovinyl)uracil (Bvura) In Vivo', Nucleosides, Nucleotides and Nucleic Acids, 4: 1, 211 — 212
**To link to this Article: DOI:** 10.1080/07328318508077856
**URL:** http://dx.doi.org/10.1080/07328318508077856

NUCLEOSIDES & NUCLEOTIDES, 4(1&2), 211-212 (1985)

# THERAPEUTIC IMPLICATIONS OF THE UNUSUALLY LONG HALF-LIFE OF (E)-5-(2-BROMOVINYL)URACIL (BVUra) IN VIVO

C. Desgranges*, G. Razaka, E.De Clercq and H. Bricaud
Unité 8 de l'INSERM, Avenue du Haut-Lévêque, 33600 Pessac, France and
Rega Institute, Katholieke Universiteit Leuven, B-3000 Leuven, Belgium

Summary - The long half-life of BVUra in the plasma permits, on the one hand, the de novo formation of the antiviral drug (E)-5-(2-bromovinyl)-2'-deoxyuridine (BVdUrd) by a pentosyl transfer, and, on the other hand, the inhibition of the degradation of pyrimidine bases such as 5-fluorouracil (FUra).



In contrast to other pyrimidine bases such as uracil (Ura), thymine (Thy), 5-iodoUra, FUra, which are eliminated from the blood stream within 2-4 hours after their administration, BVUra maintains a constant level of 50-70 μM in plasma for at least 6 hours. This peculiar behavior is probably due to the lack of degradation of BVUra by the reductive catabolic pathway of pyrimidines.

We have demonstrated that the potent and selective antiherpes agent BVdUrd[1] could be generated from BVUra in the plasma of rats following the administration of pyrimidine deoxynucleosides such as thymidine, 2'-deoxyuridine (dUrd) or other 5-substituted dUrd derivatives; BVdUrd is formed by a deoxyribosyl transfer from the deoxynucleosides to BVUra catalysed by pyrimidine nucleoside phosphorylases.[2] The generation of the active drug BVdUrd from its inactive metabolite BVUra in vivo can be repeated several times after a single administration of BVUra; and this procedure could be useful to potentiate the clinical efficacy of BVdUrd.

In addition, BVUra is an inhibitor of the reductive step of the pyrimidine catabolism and increases the in vivo half-life of other pyrimidine bases that are normally rapidly degraded, particularly of FUra; and we have demonstrated that the inhibition of FUra degradation is reflected by an increase of the antineoplastic activity of this pyrimidine analogue.



 0732-8311/85/0401-0211$3.50/0

REFERENCES

(1) De Clercq, E.; Descamps, J; De Somer, P.; Barr, P.J.; Jones, A.S.; Walker, R.T. Proc. Natl. Acad. Sci. USA 1979, 76, 2947-2951.
(2) Desgranges, C.; Razaka, G.; Bricaud, H.; Herdewijn, P.; De Clercq, E. Nucleic Acids Res. 1984, 12, 2081-2090.