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Thermal Properties and Eutectic Behaviour of Dapivirine in Combination with Steroid Hormones and Other Antiretrovirals

Karl Malcolm 1, Clare McCoy 1, Diarmaid Murphy 1, Peter Boyd 1, Sandeep Kumar 1, Susan Fetherston 1, Andrew Brimer 2, Jonathon Holt 2, Brid Devlin 2, Wendy Blanda 2, Jeremy Nuttall 2, Chris Gilmour 2
1 Queen’s University Belfast, UK, 2 International Partnership for Microbicides (IPM), USA.

It is well established that the melting point of a drug is inversely proportional to its lipophilicity (e.g. Calpeta et al., J Pharm Sci, 83 (1994) 29–33) which, in turn, correlates with its ability to be absorbed in vivo. Therefore, if the melting point of a drug can be reduced without affecting other physicochemical parameters, then drug release and/or absorption may be enhanced. This general principle has been exploited in a number of marketed pharmaceutical products, including the topical anaesthetic cream EMLA® and the contraceptive vaginal ring Nuvaring®. Both products contain two active pharmaceutical ingredients – EMLA® contains a mixture of prilocaine and lidocaine, while Nuvaring® contains etonogestrel and ethinyl estradiol. Because the equation is

\[
\begin{align*}
T & = T_0 - \frac{X_f f(A) f(B) - X_f f(A) f(C) - X_h f(A) f(B)}{X_f f(A) f(B) - X_h f(A) f(C)} \times 100
\end{align*}
\]

where

- \(T\) = zero.
- \(T_0\) = melting point of steroid A (K);
- \(X_f\) = mole fraction of solvent
- \(f(A)\) = heat of fusion of steroid A (J/mol);
- \(f(B)\) = heat of fusion of steroid B.

In order to calculate the eutectic behavior of the steroid mixtures (Dorset, 1988, 1992). Eq. (9) was used to calculate the eutectic melting point of the other drug, much in the same way that salt reduces the melting point of water (explaining its use on icy roads). For example, the phase diagram for etonogestrel and ethinyl estradiol shows that the maximum reduction in drug melting point occurs for a 1:1 mixture (Fig. 2).

During the first heating cycle, DPV shows a polymorphic transition at 105°C and a crystalline melt at 222°C. Following cooling, a second heat cycle shows a glass transition at 80°C, a recrystallisation process at 160°C and a subsequent crystalline melt at 220°C.

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According to figures E–H, the eutectic or lowest melting composition is determined as the composition having the largest heat of fusion value for the eutectic melting transition. These eutectic compositions are indicated by a dashed line.