Study of Lipophilicity Profile of Mosapride Citrate Dihydtate

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Lipophilicity profile of mosapride citrate dihydrate over a broad pH range has been determined by potentiometry. The lipophilicity of mosapride citrate dihydrate increases with the increase in pH but after pH 5.5, any change in pH does not affect the lipophilic behaviour of mosapride citrate dihydrate.

The pharmacokinetic behaviour of a drug is governed by it's physicochemical properties. Lipophilicity is one property which mainly governs the transportation of drug across the biological membranes[1]. Lipophilicity can be defined as a molecular property expressing the relative affinity of solutes for aqueous phase and organic or water immiscible phase[2]. The affinity is essential to overcome the delivery problems that limit the efficacy of a drug specially by transdermal patches or other topical routes[3]. In QSAR the biological response is correlated with the chemical structure either through physicochemical parameters or constituent contributions[4]. Lipophilicity and n– octanol:water partition coefficient, log P has been known to be one of quantitative physical properties that correlates directly with biological activity[5] and is described as one of the fundamental parameter in studies of QSAR[5]. Lipophilicity encodes most of the intermolecular forces that can take place between a solute and a solvent and represents the affinity of a molecule to the lipophilic environment. Log P values for a number of drugs have been reported[6] and predicted[7]. Various techniques can be used for the study of lipophilicity of drugs and the conventional shake flask method[8] is largely replaced by RP-HPLC[9,10] and TLC[9-12] methods. Voltametric[13] and potentiometric[14] methods are somewhat recently introduced for the study. Lipophilicity is pH dependent and as pH is not uniform in the body it is generally more relevant to ascertain the lipophilic profile of a drug over the entire pH range.

Mosapride citrate dehydrate (MCD) was launched in 1998 in India and not much data is available in literature. The lipophilicity profile of MCD was determined by potentiometry over a broad pH range in water:octanol sys-

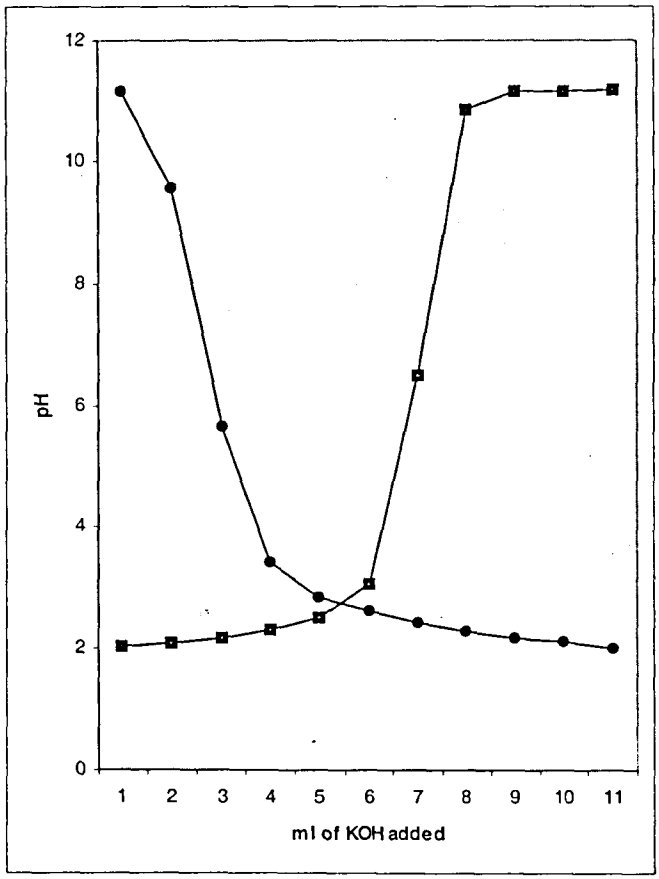

Fig. 1: Potentiometric titration of MCD with KOH

●-●-●-● indicates the titration of drug alone whereas ■-■-■-■ indicates the titration in presence of n-octanol.

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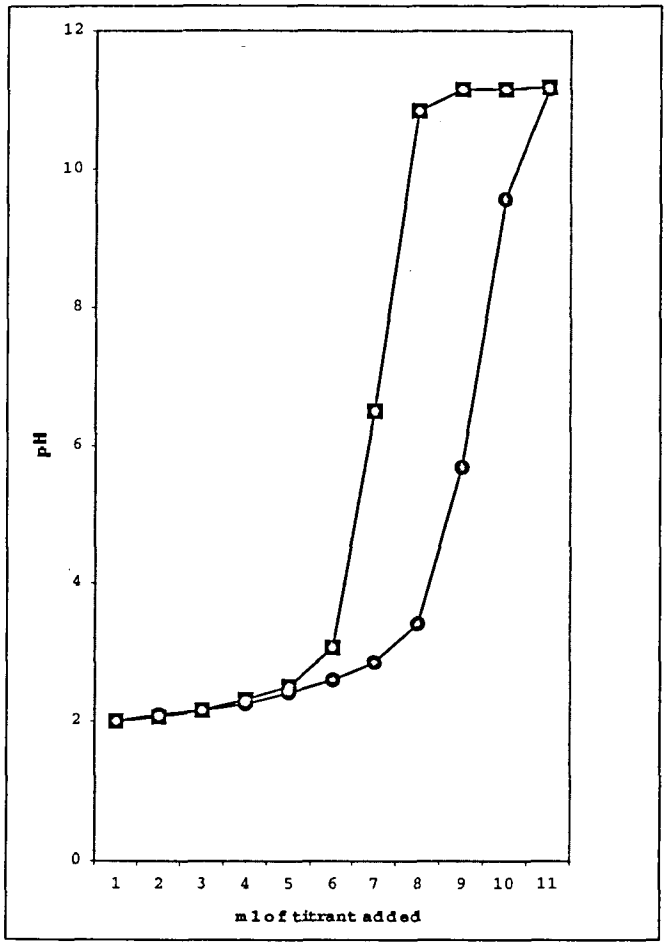

Fig. 2: Bjerrum's plot showing lipophilicity of MCD. ●-●-●-● indicates the titration of drug alone whereas ◘-◘-◘-◘ indicates the titration in presence of n-octanol.

tem. A calibrated Systronics digital pH meter 335 with combined glass – calomal electrode was used for pH measurements.

MCD was obtained as a gift sample from M/s Torrent Pharmaceuticals, Mehsana and a standard solution of MCD (0.01% w/v) was prepared in methanol:0.1 M potassium nitrate (20:80) solvent mixture. Potassium hydroxide (0.5 M), potassium nitrate (0.1 M) and 0.5 M hydrochloric acid were prepared as per IP procedure. n–Octanol was obtained from Qualigens, Mumbai.

Standard (25 ml) drug solution was titrated with 0.5 M potassium hydroxide pHmetrically to pH 11. Then 2.5 ml of octanol was added to the same solution and it was titrated back to the starting pH.

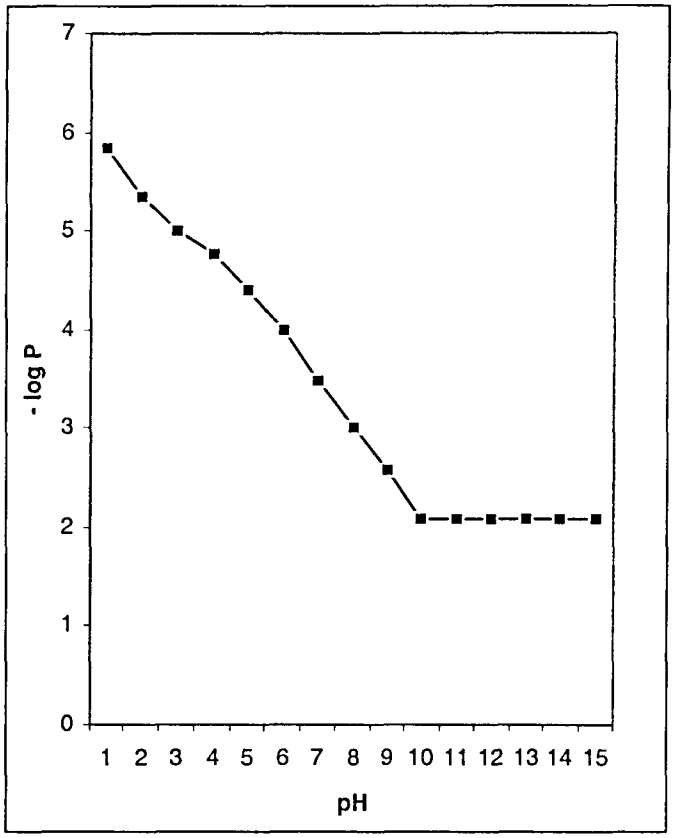

Fig.3: Lipophilicity profile of MCD. ▪-▪-▪-▪ indicates the dependence of -log P on pH.

The superimposed graphs for both these titrations showing changes in pH of the solutions with each addition of titrating agent are shown in fig. 1. In the mixture the apparent pKa was shifted from the value observed in the absence of organic phase due to partition of the drug. The extent of this shift is related to it's log P which is obtained from the calculation of the change in aqueous pH with the number of a base equivalent added to the system or from Bjerrum's plot[15] i.e. the plot of the average no. of bonded protons n_H^* as a function of pH. Bjerrum's plot for MCD is shown in fig. 2. The graph –log P vs pH was plotted (fig. 3) to get the lipophilicity profile of MCD at different pH. Lipophilicity of MCD increases as pH increase but a change in pH more than 5.5 does not affect the lipophilic behaviour of MCD.

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