Standard Scientific Research and Essays Vol1.(2): 32-35, March 2013
http://www.standresjournals.org/journals/SSRE

Research Article

Propylene glycol, polysorbate-80 and sodium lauryl sulfate as potential dermal absorption enhancers of celecoxib

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Received 15 February 2013; Accepted 24 March 2013

Abstract

The purpose of this study was to investigate propylene glycol, polysorbate-80 and sodium lauryl sulfate as potential dermal absorption enhancers of celecoxib by studying their effects on celecoxib partition coefficient. The partition coefficient was determined in chloroform-water system at room temperature. It was found that all the vehicles studied decreased the partition coefficient of celecoxib. The results suggest that propylene glycol, polysorbate-80 and sodium lauryl sulfate respectively, has the potential of decreasing the vehicle-skin partition coefficient of celecoxib and therefore are not potential vehicles for improved transdermal delivery of celecoxib.

Keywords: Celecoxib, partition coefficient, spectrophotometry.

INTRODUCTION

Celecoxib, 4-[5-(4- Methylphenyl)-3-(trifuoromethyl)-1H-pyrazol-1-yl] benezenesulfonamide is a diaryl-substituted pyrazole. Clinically, it used as an anti-inflammatory, analgesic, anti-pyretic and anti-platelet drug (Clemett, 2000; Harper, 2001). Its mechanism of action is due to inhibition of prostaglandin synthesis, primarily by inhibition of cyclooxygenase-2 (cox-2). The major drawbacks to its clinical use are gastrointestinal (GI) toxicities, gastric mucosal ulcerations, hemorrhage due to inhibition of prostaglandin production and hepatic first pass metabolism (Hawkey, 1990; Bolten, 1998; Griffin and Scheiman, 2001). This creates a need for an alternative route of administration that bypasses these drawbacks. The transdermal route is such an alternative. Several studies have reported on different techniques used in transdermal delivery of celecoxib. Such techniques include: proniosomal transdermal therapeutic gel (Alam et al., 2010), multivesicular liposomes bearing celecoxib-beta-cyclodextrin complex (Jain et al., 2007), microemulsion gel systems (Saliman et al., 2010), celecoxib nanoemulsion (Shakeel et al., 2009) and celecoxib transdermal patches (Yayaprakash et al., 2010). Propylene glycol, polysorbate-80 and sodium lauryl sulfate are often use in cosmetic or pharmaceutical formulations to serve various purposes including dermal permeation enhancement (Shen et al., 1976; Hawang and Danti, 1983; Toniton, 1986). In this work, it is designed to evaluate the influence of these vehicles on the partition coefficient of celecoxib. It is envisaged that understanding the actions of the vehicles on the partition coefficient of celecoxib will provide some knowledge on their potentials as percutaneous absorption enhancers of celecoxib. Various studies have shown that percutaneous absorption enhancers are often required in transdermal formulations to amongst other things reduce the drug dose and invariably its adverse effect. Previous report (Potts and Guy, 1992) has shown that dermal permeability coefficient depends on the partition coefficient and molecular weight of chemical substances. Furthermore, report (Bunge and Cleek, 1995) has also indicated that the partition coefficient can be used to evaluate dermal absorption of compounds. In this context, the present study investigates propylene glycol, polysorbate-80 and sodium lauryl sulfate as potential dermal permeation enhancers of celecoxib by studying the partitioning characteristics of the drug in these vehicles.

MATERIALS AND METHODS

The materials used include celecoxib (Ranbaxy Pharmaceuticals, India), propylene glycol, polysorbate-80 and sodium lauryl sulfate were purchased from Sigma-Aldrich (USA), chloroform was purchased from Fisher Scientific (USA) and other chemicals were of analytical reagent grade.

Standard solution

Stock solution of celecoxib (50 μg/ml) was prepared in methanol. Aliquots (5.0-25.0 μg/ml) of the standard stock solution were pipetted into a 10 ml volumetric flask diluted to volume with methanol.

Partition coefficient measurement

The partition coefficient of celecoxib was determined in a chloroform-water system. To 5 ml of chloroform (saturated with different vehicles studied) containing 500 μg of celecoxib was added 5 ml of aqueous solution (saturated with chloroform) of different concentrations of propylene glycol, polysorbate-80 and sodium lauryl sulfate. The flasks were capped and agitated at room temperature for 2 h to achieve complete equilibration. The phases were analyzed spectrophotometrically using UV/Vis spectrophotometer (Jenway 6305, England) at a maximum wavelength of 251 nm. The drug concentration was obtained from a pre-constructed calibration graph. The partition coefficient of celecoxib was calculated using this equation (Johansen and Bundgaard1, 980a):

$P = C_oV_w / C_wV_o$,

where P is the partition coefficient; C_o is the concentration of celecoxib in organic phase; C_w is the concentration of celecoxib in aqueous phase; V_w is the volume of the aqueous phase; V_o is the volume of organic phase.

RESULTS AND DISCUSSION

The calibration graph of celecoxib was linear and obeyed Beer's law in the concentration range of 5.0-25.0 μg/ml. Absorbance versus concentration relationship is described by regression equation: A = 0.0485C - 0.014 (r = 0.9985). The results of the influence of propylene glycol, polysorbate-80 and sodium lauryl sulfate on the partition coefficient of celecoxib are shown in Table 1.

Table 1: Effect of propylene glycol, polysorbate-80 and sodium lauryl sulfate on the partition coefficient of celecoxib and estimated permeability coefficients.

Concentration of binary mixture (% w/v)	Propylene glycol		Concentration of micellar solution (% w/v)	Polysorbate-80		Sodium lauryl sulfate	
	log P	log K_p		log P	log K_p	log P	log K_p
0.0	3.678	- 2.415	0.00	3.678	-2.415	3.678	- 2.415
5.0	3.576	- 2.487	0.05	3.598	- 2.472	3.537	- 2.515
10.0	3.492	- 2.547	0.10	3.486	-2.551	3.315	- 2.673
15.0	3.412	- 2.604	0.20	3.345	-2.652	3.032	- 2.874
20.0	3.328	- 2.664	0.40	3.231	-2.732	2.784	- 3.050
25.0	3.275	- 2.701	1.00	3.009	-2.890	2.456	-3.283

All the vehicles investigated decreased the partition coefficient of celecoxib with sodium lauryl sulfate producing the highest decreasing effect. The decreasing effect was observed as the concentration of the vehicle was increased. For example, at the concentration level of 30% w/v (propylene glycol), 1.0% w/v (polysorbate-80 and sodium lauryl sulfate respectively), the logarithm partition coefficients of celecoxib are 3.187, 3.009 and 2.456 for propylene glycol, polysorbate-80 and sodium lauryl sulfate respectively. Decrease in dielectric constant of propylene glycol-water systems could explain the effect of propylene glycol on the partition coefficient of celecoxib. With the micellar solutions, the decrease in the partition coefficient of the drug observed with polysorbate-80 could be due to the entrapment of the drug in the micelles, thus retarding the partitioning of celecoxib out of micellar solution into the organic phase (chloroform). However, the decrease in the partition coefficient seen with sodium lauryl sulfate could be as a result of micellar entrapment as well as the pH effect. The pH effect arises from the ionization of celecoxib (acidic drug) in sodium lauryl sulfate solution and thus greater affinity for the aqueous phase than the organic phase. A plot of concentration of propylene glycol-water system versus the logarithm observed partition coefficient is shown in Figure 1, while Figure 2 represents that of micellar solution. In all the plots, a close linear relationship was

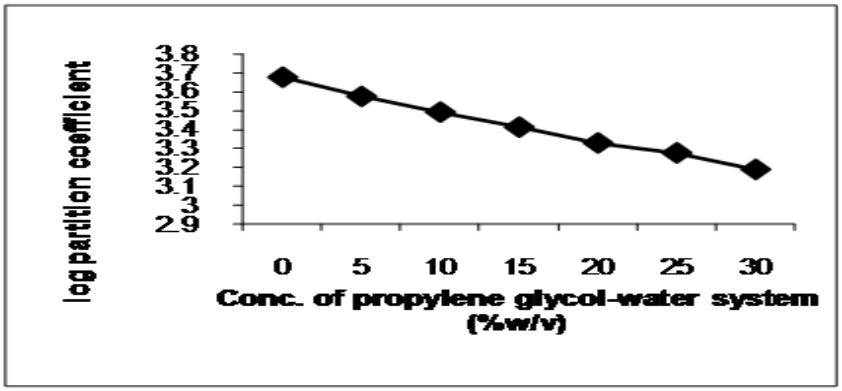

Figure 1. Plot of logarithm partition coefficient of celecoxib versus propylene glycol-water system.

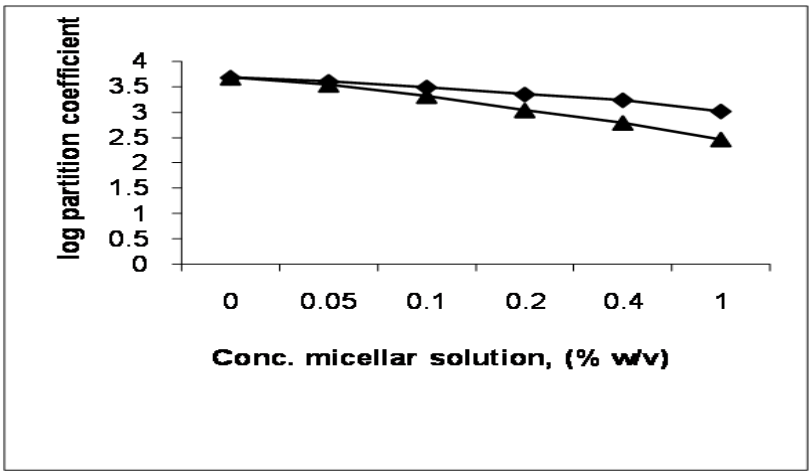

Figure 2. Plot of logarithm partition coefficient of celecoxib versus micellar concentration. (□) polysorbate-80; (Δ) lauryl sulfate.

obtained with correlation coefficients of –0.9976, -0.9370, -0.9167 for propylene glycol, polysorbate-80 and sodium lauryl sulfate respectively. The logarithm observed partition coefficient values were used to estimate the dermal permeability coefficient of celecoxib through the skin using previously reported equation (Potts and Guy, 1992):

$\log K_p$ (cm/h) = -2.7 + 0.17 log P – 0.0061 MW

where $\log K_p$ is the logarithm dermal permeability coefficient of celecoxib; log P is the observed logarithm partition coefficient of celecoxib; MW is the molecular weight of celecoxib. The results are shown in Table 1. Previous report (Korinth et al., 2005) has shown permeability coefficient to be a useful parameter in evaluating percutaneous absorption. With the micellar solutions, the K_p value of celecoxib at the concentration level of 1.0 % w/v, showed polysorbate-80 having a factor of about 2.5 much higher than sodium lauryl sulfate.

CONCLUSION

The estimated permeability coefficients indicated that the order of dermal permeation enhancement is propylene glycol> polysorbate-80 >sodium lauryl sulfate. Finally, the results suggest that these vehicles are not potential percutaneous absorption enhancers of celecoxib.

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