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Higuchian Matrix Mechanism from Transdermal Matrix System of Aceclofenac

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ABSTRACT

Transdermal Therepeutic system (TTS) was prepared by film casting technique.The mercury surface was selected for film formation. The dried films were removed from the glass ring and kept in a desiccator until use. The optimized formulation of Aceclofenac was selected for the determination of mechanisms of drug release. Cumulative percent of drug released was plotted against square root of time which indicated the release and permeation pattern as anticipated by Higuchian matrix mechanism of drug release.

Keywords: Transdermal, First order, Higuchi mechanism

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METHODOLOGY

Plasticizers and polymers were dissolved in the solvent and poured into the film casting assembly i.e. glass rings placed on the surface of mercury in a petridish [1-3]. Solvent was allowed to evaporate by placing an inverted funnel over the petridish which controlled the rate of evaporation of the solvent. The optimized formulation of Aceclofenac was selected for the determination of mechanisms of drug release and permeation. In order to determine these parameters, the cumulative percentage of drug released and permeated was plotted against square root of time (Fig. 1& 2).

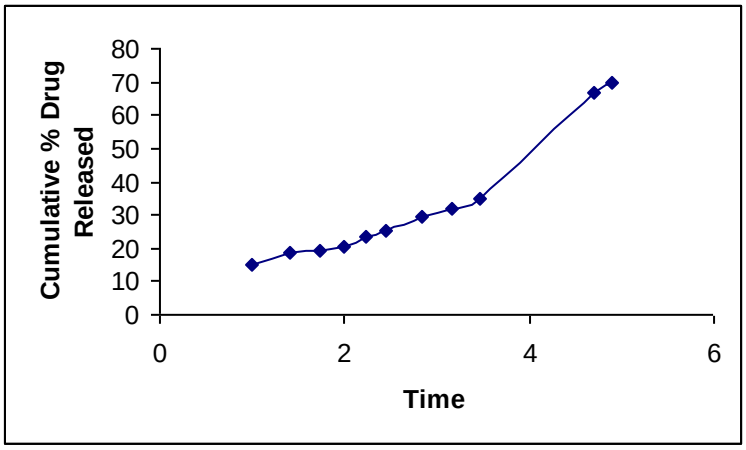

Fig.1: Plot of cumulative % of Drug Released vs. Square Root of time

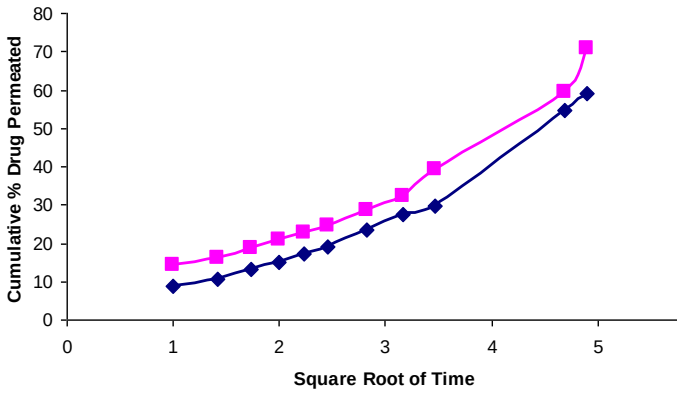

Fig. 2: Plot of cumulative % of Drug Permeated vs Square Root of time (Two optimized Formulations)

The rate constants for zero order and first order release and permeation were calculated for each time interval using the following formulae in order to assess the order of drug release and permeation from TTS [4-6].

For zero order rate constant,

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$$K_0 = \frac{\%\ \text{drug released or permeated}}{\text{Time (h)}}$$

For first order rate constant,

$$K_1 = \frac{2.303}{t} \log \frac{Co}{C}$$

Where, Co = initial percentage of drug (100%)
C = percentage of drug remaining at time "t"

Results are given in Table 1 to 2.

Table 1: Kinetic Analysis of *in vitro* Drug Release Data for Optimized Formulation

Time (h)	Cumulative % of drug released	% of drug remaining	Zero Order K_o	First Order K_1 (h^{-1})
1	15.1278	84.8722	15.1278	0.164
2	18.38234	81.61766	9.19	0.101
3	19.20578	80.79422	6.40	0.071
4	20.42135	79.57865	5.105	0.057
5	23.44061	76.55939	4.688	0.053
6	25.32277	74.67723	4.22	0.048
8	29.43996	70.56004	3.67	0.043
10	31.87106	68.12894	3.187	0.038
12	35.12562	64.87438	2.92	0.036
22	66.92605	33.07395	3.04	0.050
24	69.63163	30.36837	2.901	0.049
COV for K_o = 67.55		Average	5.493	0.064
COV for K_1 = 57.81		S.D.	3.711278	0.037633

Coefficient of variation (COV) = S.D/Average x 100

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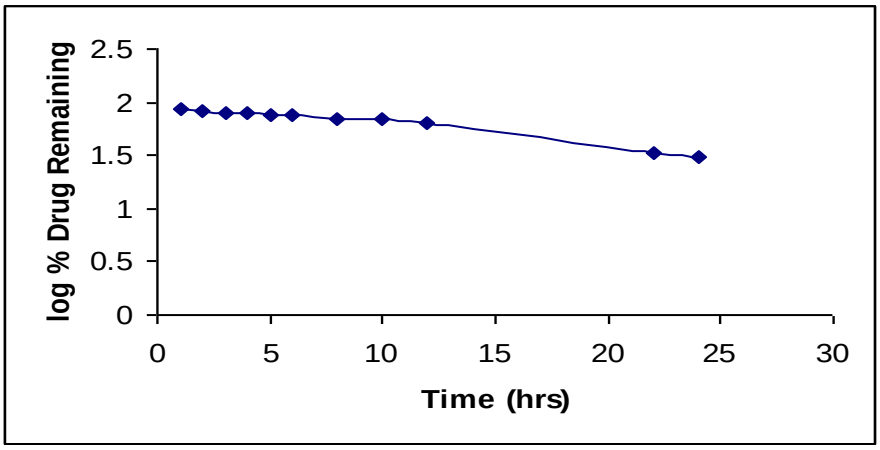

Fig. 3: Determination of Order of Release of Drug from Optimized Formulation.

Table2: Kinetic analysis of *in vitro* Skin Permeation Data of Optimized Formulation

Time (h)	Cumulative % of drug permeated	% of drug remaining	Zero Order K_o	First Order K_1 (h^{-1})
1	8.811273	91.19	8.811	0.092
2	10.72828	89.28	5.36	0.056
3	13.09839	86.91	4.36	0.046
4	15.15481	84.85	3.78	0.0410
5	17.24608	82.76	3.44	0.0378
6	19.02367	80.98	3.17	0.0351
8	23.38049	76.62	2.92	0.033
10	27.45848	72.55	2.74	0.0320
12	29.68916	70.32	2.47	0.0293
22	54.61018	45.39	2.48	0.0359
24	59.00186	41.00	0.40	0.0371
COV for K_o = 58.45		Average	3.630	0.04752
COV for K_1 = 37.26		S.D.	2.122168	0.017793

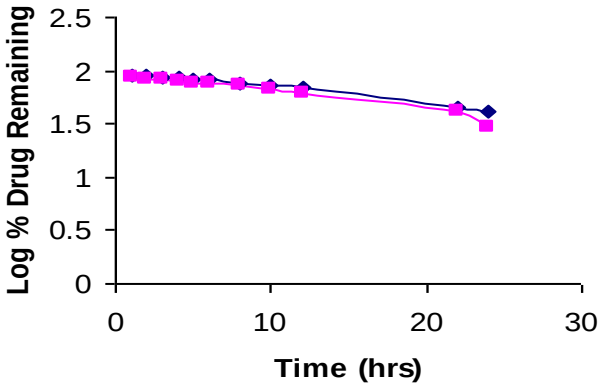

Fig. 4: Determination of order of Skin Permeation of Aceclofenac from Optimized Formulation

Coefficient of variation (COV = S.D/Average of order x 100) was also calculated for the rate constants in each case and plots of log % drug remaining V/s time were also constructed (Fig. 3 & 4) [7-8].

CONCLUSION

The data of the optimized formulation were then subjected to analysis in order to determine the mechanism of drug release and permeation from the TTS. Cumulative percent of drug released was plotted against square root of time, which followed the release and permeation pattern as anticipated by ***Higuchian matrix mechanism*** of drug release.

Kinetic analysis was also carried out, for the optimized formulation, in order to determine the release and permeation rate constants. Release and permeation rate constants were calculated for zero order and first order rate kinetics for different time intervals and coefficient of variation was calculated. A decrease in coefficient of variation was observed for first order rate kinetics as compared to zero order indicating that the release and permeation of drug through the patch formulation occurred by first order rate kinetics.

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