Short Communication
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ASSESSMENT OF SHELF LIFE FOR THE ACECLOFENAC PATCH

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ABSTRACT
The matrix type Transdermal drug delivery system of aceclofenac was prepared by film casting technique employing mercury as the substrate. Stability studies for optimized formulations were carried out according to ICH guidelines. The optimized formulations were subjected to accelerated stability studies. Sufficient replicates of formulation were prepared, packed in aluminium foil and stored in petri dishes at temperature of 40± 0.5°C, 50± 0.5°C and 60± 0.5°C for 60 days. Samples were withdrawn at intervals of 15, 45 and 60 days and analyzed for drug content by HPLC method. The shelf life of formulations of aceclofenac were determined by accelerated stability studies on the basis of first order degradation kinetics and $t_{0.9}$ (the time required to degrade 10 % of drug at 25°C). The shelf life was found to be 1.158yrs.
Keywords: Aceclofenac, Patch, Stability studies, Shelf life.

INTRODUCTION

The most commonly used transdermal delivery system is transdermal patch. However, developing a transdermal therapeutic system and the subsequent penetration of the drug candidate in therapeutic amounts through the skin represent a significant challenge. This is especially true because transdermal patch should combine both pharmaceutical cosmetic and stability qualities. Stability studies for optimized formulation were carried out according to ICH guidelines[1-3].

The ICH guidelines entitled "stability testing of new drug substances and products" require that stress testing be carried out to elucidate the inherent stability characteristics of the active substances. It suggested that the degradation products that are formed under a variety of conditions should be identified and degradation pathway established. It is stated that testing should include the effect of temperature, humidity (where appropriate); oxidation, photolysis and susceptibility to hydrolysis across a wide range of pH values. The study of effect of temperature is suggested to be done in 10°c increments above the accelerated temperature test condition (e.g., 50°, 60° etc) and that of humidity at a level of 75% or greater.

METHODOLOGY

The HPLC method was performed according to Ph Eur monograph 1281, with slight modification as per our system availability. The system consisted of Thermofinangn with a UV detector (Model: Surveyor autosampler plus). In this method Acetonitrile: Water (9:1):: Phosphoric acid (70::30) optimized as a mobile phase plus diluent and a 10 cm X 4.6 mm RP C_{18} Hypersil gold column having a 5µm packing as a stationary phase. Flow rate of 1.0 ml/min, Detection at 275 nm, Injection volume of 10 µl was used.

Ten different concentrations of aceclofenac ranging from 2– 20 µg/ml were prepared for linearity studies (Table 1). The responses were measured as peak areas and plotted against concentrations to prepare a calibration curve (Figure 1).

The logarithm of % drug remaining was plotted against time in days (Figure 2), which gave almost straight line suggesting that drug degradation followed first order kinetics. The slope of the straight line for each temperature was obtained and the degradation rate constant was calculated using the formula given below:

$$\text{Slope} = -K/2.303$$

Where, K is degradation rate constant.

An Arrhenius plot was drawn by plotting logarithm of K values against reciprocals of absolute temperature (Figure 3). The value of K at 25°C (K_{25}) was extrapolated from the Arrhenius plot and shelf-life of the formulation was calculated by substituting the vales of K_{25} in the following equation[1, 3-5]:

$$t_{0.9} = 0.1054/K_{25}$$

Where, $t_{0.9}$ is the time required for 10% degradation of the drug and is referred to as the "Shelf-life" of the product.

The degradation rate constant at various temperatures and the shelf life of the formulation is reported in Table 2.

Table 1: Concentration and the Area obtained for construction of calibration curve

Concentration (µg/mL)	Area	S.D. (n=3)
2	52000	± 37
4	100000	± 125
6	180000	± 306
8	280000	± 1105
10	380000	± 1285
12	460000	± 1956
14	570000	± 2384
16	699443	± 5695
18	810000	± 6820
20	900000	± 10785

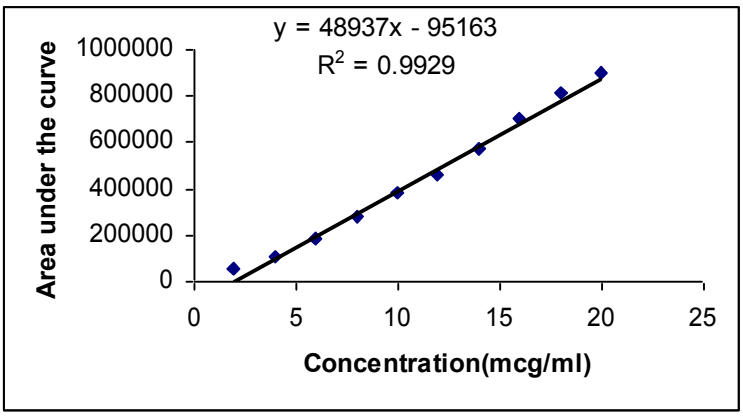

Figure 1: Calibration curve of aceclofenac by HPLC method

Table 2: Degradation of aceclofenac in Patch Formulation at different temperatures

Temperature								
40 ± 0.5°C			50 ± 0.5°C			60 ± 0.5°C		
Drug Content (mg)	% Drug Remaining	Log % Drug Remaining	Drug Content (mg)	% Drug Remaining	Log % Drug Remaining	Drug Content (mg)	% Drug Remaining	Log % Drug Remaining
36.2	100	2	36.9	100	2	36.3	100	2
36.04	99.57	1.99812	36.66	99.37	1.99725	35.98	99.14	1.99624
35.89	99.16	1.99633	36.42	98.71	1.99436	35.69	98.34	1.99273
35.63	98.45	1.99322	36.16	98.01	1.99127	35.34	97.36	1.98838

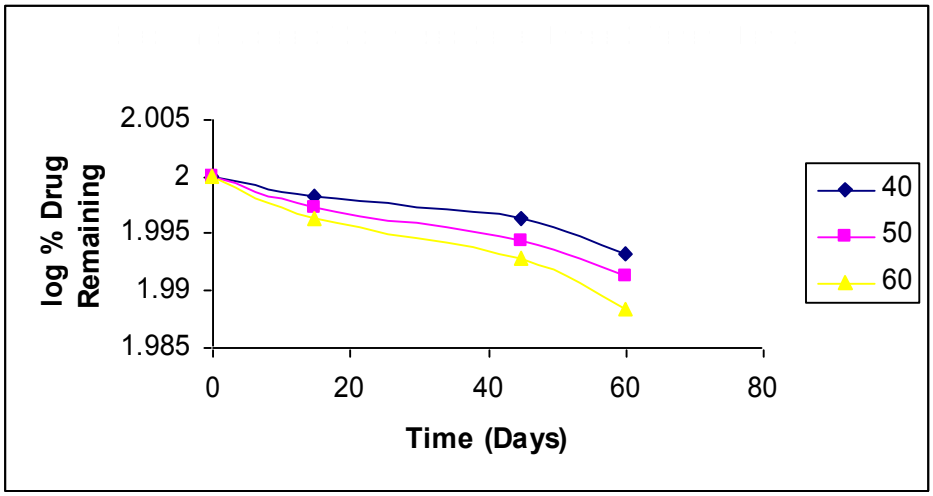

Figure 2: Degradation Kinetics of aceclofenac Formulation

Table 3: Degradation Rate Constants Determined at Various Temperatures and Shelf-Life of aceclofenac

Temperature (°C)	Slope X 10^{-4}	K (Day^{-1}) X 10^{-4}	Log K + 5	Absolute Temperature T (K)	1/T x 10^{-3} (K^{-1})	Shelf-life at 25°C (Year)
40	-1.026	2.362	1.3732	338	2.95	1.158
50	-1.356	3.122	1.4944	348	2.87	
60	-1.783	4.106	1.6134	358	2.79	
Value at 25°C		2.533	1.4036	323	3.095	

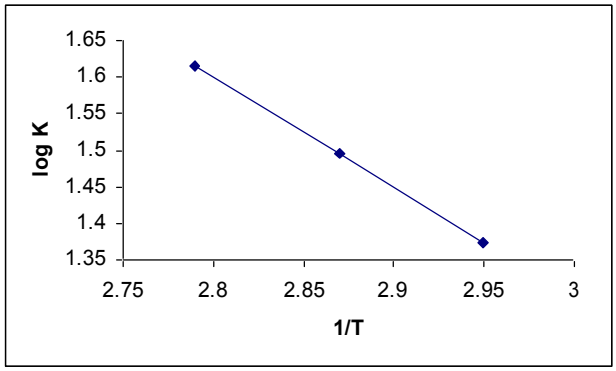

Figure 3: Arrhenius plot for optimized aceclofenac patch

CONCLUSION

In this study, the shelf life of transdermal formulations of Aceclofenac was found to be 1.158 yrs.

REFERENCES

1. Carstensen JT. Drug stability: principle and practices, Marcel Dekker Inc.; 1990;43: 125-142.
2. Ph Eur monographs 1281 4th Ed.: 2002, 572-573.
3. Arora P, Mukherjee B. Design, Development, Physicichemical, and in-vitro and in- vivo Evaluation of Transdermal Patches containing Diclofenac diethylammonium salt. J Pharm Sci 2002; 9: 2076-2089.
4. Bakshi M and Singh S. Development of validated stability-indicating assay methods- critical review. J Pharmaceut Biomed Analys 2002; 28: 1011-1040.
5. FDA, guideline for submitting documentation for stability of human drugs and biologics. Food and drug administration, Rockville; 1987.
6. ICH, stability testing of new drug substances & products, International Conference on Harmonization, IFPMA, Geneva; 1993.
7. ICH, test on validation of analytical procedure, International Conference on Harmonization, IFPMA, Geneva; 1994.
8. ICH, impurities in new drug substances, International Conference on Harmonization, IFPMA, Geneva; 1995.
9. ICH, quality of biotechnological products: stability testing of biotechnological/ biological products, International Conference of Harmonization, IFPMA, Geneva; 1995.
10. ICH, impurities in new drug products, International Conference on Harmonization, IFPMA, Geneva; 1996.
11. ICH, stability testing photostability testing of new drug substances of products, International Conference on Harmonization, IFPMA, Geneva;1996.
12. ICH, validation of analytical procedure, International Conference on Harmonization, IFPMA, Geneva; 1996.
13. ICH, specification test procedure and acceptance criteria for new drug substances and new drug products chemical substances, International Conference on Harmonization, IFPMA, Geneva; 1999.
14. ICH, good manufacturing practice for active pharmaceutical ingredients. International Conference on Harmonization, IFPMA, Geneva; 2000.
15. ICH, stability testing of new drug substances and products, International Conference on Harmonization, IFPMA, Geneva; 2000.

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