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Kinetics of Degradation of Sulphasalazine in Aqueous Solution

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The degradation kinetics of sulphasalazine was studied in aqueous solution at room temperature in the pH range of 3–12 with an ionic strength of 0.2 μ. The degradation rates were determined by quantitative thin layer chromatographic and spectroscopic methods. The degradation of the drug is of first order and has a maixmum stability at pH 5.7.

INTRODUCTION

Sulphasalazine is used in the treatment of polyarthritis as well as for ulcerative colitis[1, 2]. A survey of the literature indicates that no studies have been attempted to understand the mechanism of degradation of sulphasalazine. The value of this study lies in the fact that of the two main metabolic products of sulphasalazine namely 5-amino salicylic acid and sulphapyridine, the latter metabolite is thought to be responsible for most of the adverse effects[3].

The present research was undertaken to study in detail the stability kinetics of sulphasalazine in aqueous solution and to understand the mechanism of hydrolysis of the drug *in vitro* under various pH conditions which, in turn, can be correlated to degradation of the drug *in vivo*. The results can be utilized in designing new forms for the drug.

EXPERIMENTAL

Pure sulphasalazine was obtained from Wallace Pharmaceuticals, Mumbai.

The buffers prepared were: HCl-KCl (pH 2.8–4.0); phosphate-NaOH (pH 5.1–7.0); boric acid—NaOH (pH 7.9–9.0) and phosphate—NaOH (10.8–11.8)[4]. The ionic strength was maintained at 0.2 μ with KCl. All other reagents were of analytical grade. An Elico L 10T pH meter amd a Cary-17D UV-visible spectrophotometer was used.

Determination of percentage purity of sulphasalazine

A procedure similar to that described in USP was adopted[5]. The purity of the drug was found to be 99.28 ± 0.493%.

Determination of λ_{max} in different pH solutions

The above procedure was utilized. The λ_{max} was found to be same in the acidic and basic pH and confirmed with the reported results to be 360 nm.[5]

Calibration curve in different pH solutions by spectrophotometric method

75.0 mg of sulphasalazine was dissolved in 50 mL. of 0.1N NaOH solution to obtain a 1.5 mg/mL stock solution, from which volumes of 0.025, 0.075, 0.1, 0.125, 0.150, 0.075 and 0.2 mL were transferred into seven different 25 mL volumetric flasks. To each of these solutions 0.5 mL of 0.1 N CH_3COOH was added and final volumes made up to 25 mL to obtain concentrations of 1.5, 3.0, 4.5, 6.0, 7.5, 9.0, 10.5 and 12.0 μg/mL respectively. This procedure was repeated for all pH solutions. Absorbances of the final solutions were determined at 360 nm using respective buffer solutions as blanks.

Stability studies by spectroscopic method

The stability studies were followed by spectrophotometric method according to the methodology described in the literature[6–8] and were modified to suit this study. Eight samples of drug solutions with a final concentration of 6.0 μg/mL in eight different buffers from pH range 2.71 to 11.56 were prepared and their absorbances determined at 360 nm using respective buffer solutions as blanks for a period of 20 days. The absorbances were converted into concentrations from the standard graphs obtained for each buffer solution.

RESULTS AND DISCUSSION

The degradation of a drug may be catalysed either by an acid or a base. The mechanism of degradation of a drug can be studied *in vitro* and the kinetic parameters involved in predicting the stability of the drug can be determined. The *in vitro* study can be correlated to the degradation of the drug *in vivo*. When a drug is administered through an oral route it passes through a number of regions with a wide variation of pH (saliva—pH 6.8; stomach—pH 2.1; small intestine—pH 5.7; large intestine—pH 6.8). Therefore, depending upon the nature of the catalysis of the drug, it may degrade in any of these regions.

TABLE-1
RESULTS OF STABILITY STUDIES FOR SULPHASALAZINE BY SPECTROPHOTOMETRIC METHOD

pH	Concentration									
	TIME (DAYS)									
	0	1	4	9	10	11	14	16	17	20
2.71	100	97.80	99.2	100.2	102.8	98.15	99.4	89.7	89.0	89.2
3.93	100	89.20	98.2	98.7	102.7	91.20	91.2	83.5	90.2	90.0
4.93	100	96.80	100.0	98.6	106.1	97.61	104.0	105.3	109.2	106.6
5.90	100	100.00	92.2	90.5	103.6	100.20	109.0	78.5	102.4	88.6
7.01	100	94.88	98.7	104.8	113.8	105.60	97.4	102.3	107.9	109.2
8.11	100	98.68	101.3	105.5	109.6	113.40	111.2	114.8	122.5	120.0
9.05	100	89.10	100.0	99.2	102.2	102.50	102.7	101.5	108.5	107.6
11.60	100	93.60	112.0	100.8	85.6	96.80	96.0	95.2	86.4	84.0

Two methods were utilized for the analysis of kinetics of degradation of sulphasalazine in this study. The quantitative thin-layer chromatographic (TLC) method was used because it involves the isolation of the drug as a result of which the impurities or the degradation products of the drug are eliminated. These impurities

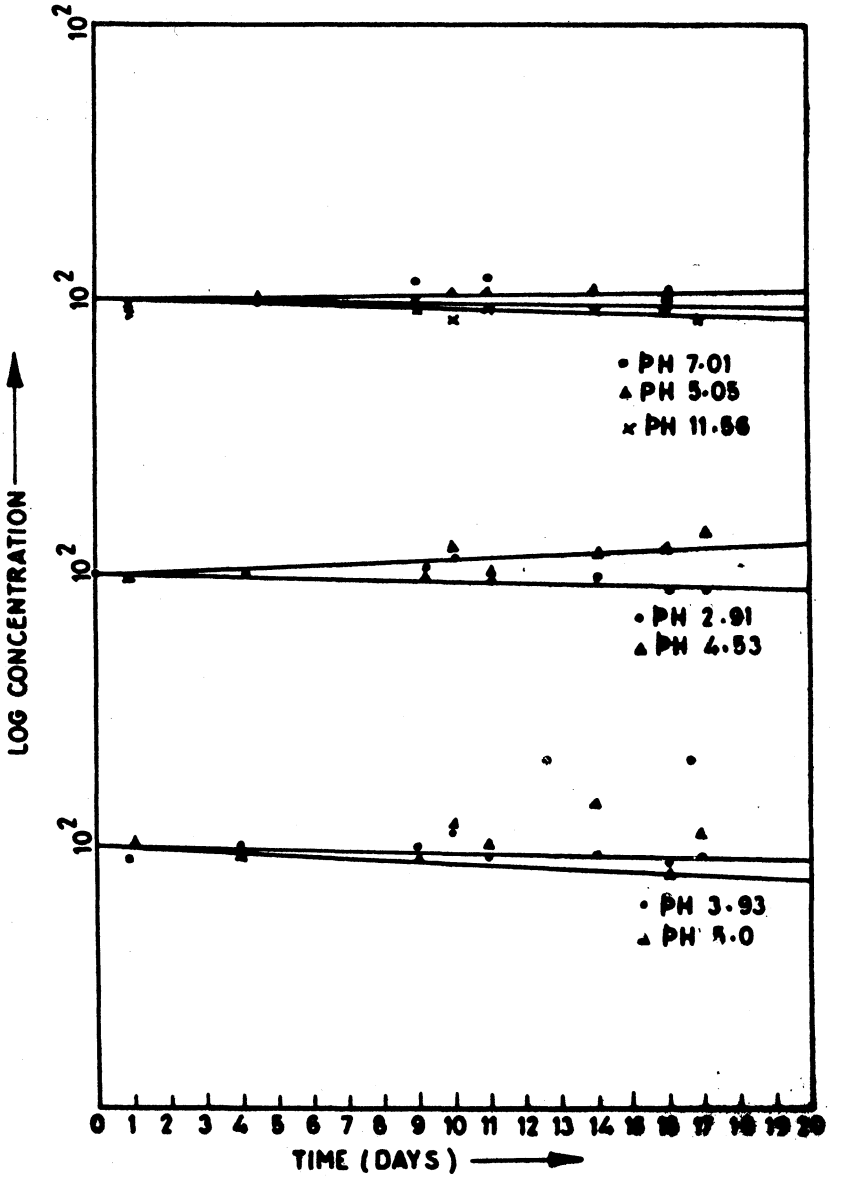

Fig. 1. log concentration time profile for sulphasalazine

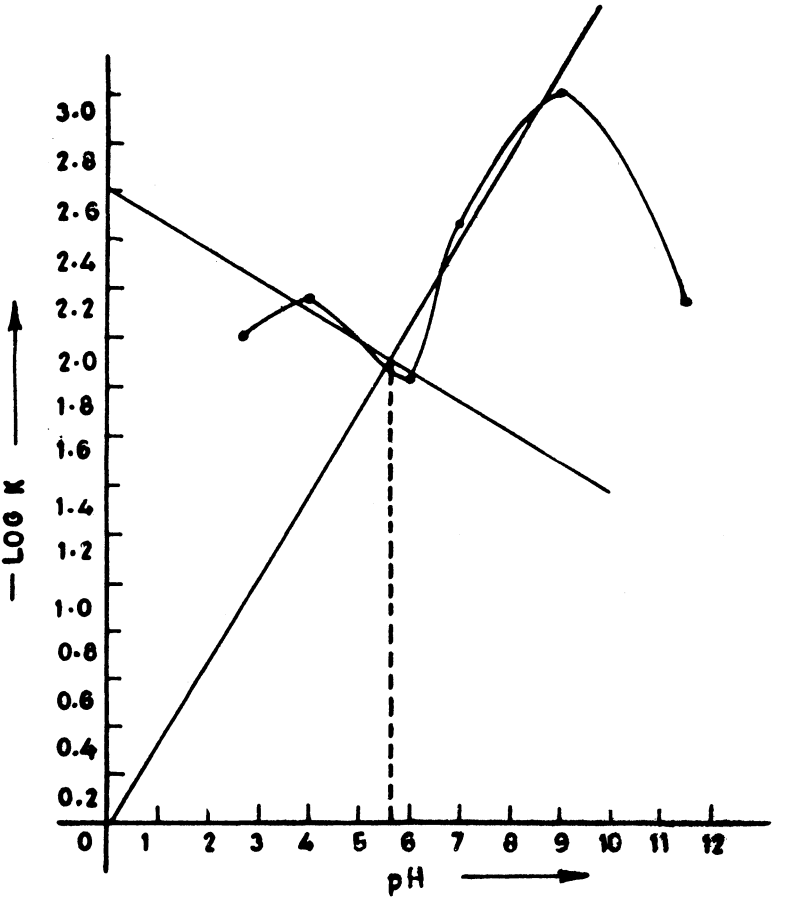

Fig. 2. pH rate profile for sulphasalazine

show absorbance along with the drug when analysed by the spectrophotometric procedure.

Calibration curves were successfully obtained for all pH solutions by the spectrophotometric procedure. The absorbances obtained were converted into the concentrations (Table-1). The necessary calculations were performed (Table-2) and graphs plotted (Fig. 1). The graph between the concentration remaining versus time was not a straight line which meant that the degradation of the drug did not follow a zero order kinetics. Therefore, log concentration remaining versus time was plotted. Using the first order equation of $C = \log C_0 - kt/2.303$ where C is concentration. A plot of log C versus t resulted in a straight line with slope as $-k/2.303$. The value of k was calculated from the graph for all pH solutions. The degradation of the drug followed a first order kinetics and also showed maximum stability at pH 5.7 (Fig. 2).

TABLE-2
RESULTS OF DEGRADATION RATE CONSTANTS FOR SULPHASALAZINE

pH	Slope = -k/2.303	K	-log K
2.71	-2.51×10^{-3}	0.0057	2.24
3.93	-3.18×10^{-3}	0.0073	2.15
4.93	1.297×10^{-3}	0.0030	—
5.90	-6.8×10^{-3}	0.0150	1.82
7.01	-1.49×10^{-3}	0.0034	2.46
8.11	—	—	—
9.05	4.7×10^{-3}	0.0100	-2.96
11.56	-3.11×10^{-3}	0.0071	2.14

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