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Short Communication

Metabolism of Aspirin in Healthy Males

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ABSTRACT

The metabolism of aspirin in young males having age between 20-23 years was studied. The volunteers were given an oral dose of 600 mg aspirin. Urine samples were collected at predetermined time interval. The concentration of major metabolite of acetyl salicylic acid (Salicyluric acid) was determined spectrophotometrically. pH of urine was 6.24±0.11; concentration of salicyluric acid (SU) was 200.5±14.9 µg/mL and value for per cent cumulative amount excreted was 31.81±1.32%.

Key Words: Aspirin; Metabolism; Male; Salicyluric Acid

INTRODUCTION

Aspirin apart from its side effects is abundantly consumed as pain reliever due to its prompt action. It is available in different formulations with different brands as dispirin, disprol, and entericoated aspirin. So it is very important to study the kinetics of the drugs for the evaluation of their beneficial effects. Aspirin on hydrolysis in stomach and blood yield salicylic acid and acetic acid. Its biological half life is 20 min. The half life of salicylate is 2-4.5 h if followed by therapeutic doses. But its overdose increases the half life to 18-36 h (Done, 1960). Approximately 80% of salicylic acid is metabolized in the liver. Salicylic acid in conjugation with glycine, forms salicyluric acid and with glucuronic acid forms salicyl acyl and phenolic glucuronide. These metabolic pathways have only a limited capacity. Small amounts of salicylic acid are also hydroxylated to gentisic acid. With large salicylate doses the kinetics switch from first order to zero order.

Salicylates are excreted mainly by the kidney as salicyluric acid (75%), free salicylic acid (10%), salicylic phenol (10%), acyl glucuronides (5%) and gentisic acid (<1%), when small doses (less than 250 mg in an adult) are ingested, all pathways proceed by first order kinetics, with half life of about 2-3 h. When higher doses of salicylate are ingested (more than 4 g), the half life becomes longer (15-30 h) (Haretwing-Otto, 1983).

It is affirmative to analyze its metabolites and urinary excretion in healthy males after its oral administration and to provide correct informations under local conditions. Female volunteers showed different metabolites and rate of excretion (results not shown). The present project was designed to evaluate the urinary excretion of acetylsalicylic acid (aspirin) in healthy males under local environmental conditions.

MATERIALS AND METHODS

The experiment was conducted on 12 healthy males in the Department of Chemistry, University of Agriculture, and Faisalabad. Mean age, weight and height of the participants were 23.3 years, 66.8 kg and 159.39 cm, respectively. Sampling was done in December. Medication of any type was disallowed to volunteers seven days before the beginning of trials. Drug free urine samples were collected before oral administration. Aspirin (600 mg) was given to each volunteer orally after an overnight fastening. Subjects were allowed to take breakfast after 2 h of oral dose.

Collection of urine samples. The urine samples of each volunteer were collected at 30, 60, 120, 180, 240, 360 and 600 min after oral intake of aspirin. The pH of all fresh urine samples was determined at 36-37^{o}C. Each urine sample was stored in plastic bottles kept at -20^{o}C for further analysis.

Urine analysis. The concentration of salicyluric acid (SU) in the urine was determined by a validated colorimetric method (Farid *et al.*, 1975). It was based on the selective extraction of salicyluric acid (SU). Salicyluric acid was extracted from 2 mL of urine (acidified with HCl) by 10 mL carbon tetrachloride and ethylene dichloride. The extracts of each solvent were shaken with 5 mL of ferric nitrate solution (10-fold dilution of 17 g of $Fe(NO_3)_3.9H_2O$ in 1L of 70 m mol/L HNO_3). The colored aqueous phase was centrifuged at 3000 rpm and absorbance was taken by spectrophotometrically (Model Hitachi U-2001) at 530 nm. Control was prepared (1ml of distilled H_2O + 5 mL of 0.17% Fe $(NO_3)_3$reagent) and spectrophotometer was calibrated by running blank.

Calculations. Calculation was made by determining the concentration of drug, %age dose excreted and also the %age of cumulative dose excreted.

Table I. Concentration and percentage cumulative dose of salicyluric acid excreted (µg/mL) after oral administration of (2 x 300 mg) aspirin

	Time (min)					
Parameters	**30**	**60**	**120**	**180**	**240**	**600**
Concentration	68.3±15	177.6±43.7	114±15.1	237.6±62.5	363.8±18.6	393±78.8
% Cumulative Dose	1.6±0.39	5.4±0.84	15.2±1.5	31.6±3.11	43±3.81	59.1±1.1

$$Concentration\ of\ drug\ (\mu g / mL) = S\tan dard\ Factor \times Absorbance$$

Statistical analysis. The results were tabulated and subjected to statistical analysis (Steel & Torrie, 1992).

RESULTS AND DISCUSSION

The results are presented in Table I. The results of pH recorded in the present study are comparable to urine pH 6.5±0.7 for males volunteers after giving 900 mg oral dose of drug as reported by Hutt *et al*. (1986). The concentration of salicyluric acid excreted in urine of male volunteers was 200.5±14.9 µg/ml. The concentration of drug also depends upon pH of the fluid and pka of drug. pH is an important parameter which differs among local and foreign species (Nawaz, 1994). Weak acids are excreted more rapidly in alkaline medium primarily because they are more ionized and passive reabsorption is decreased and vice versa. The difference in the amount of salicyluric acid excreted is mainly due to dose but pH of urine and other environmental factors may also affect.

The mean cumulative percent dose excreted as free salicyluric acid in the present study is 31.81±1.32% (Table I). This difference may be due to fluctuation in urine pH, environmental conditions and nutritional ingredients (Nawaz, 1994).

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