Effect of *Tamarindus indica* L on the Bioavailability of Ibuprofen in Healthy Human Volunteers

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**SUMMARY**

The influence of *Tamarindus indica* L fruit extract incorporated in a traditional meal on the bioavailability of Ibuprofen tablets 400mg dose when given concurrently was studied in 6 healthy human volunteers. There was a statistically significant increase in the plasma levels of Ibuprofen and its metabolites hydroxy-ibuprofen and carboxy-ibuprofen respectively, when the meal containing *Tamarindus indica* fruit extract was administered with the ibuprofen tablets than when taken under fasting state or with the meal without the fruit extract. The \( C_{\text{max}} \), \( \text{AUC}_{0-6h} \) and \( K_{\text{a}} \) for ibuprofen increased from 38 ± 0.70 \( \mu g/ml \) to 42 ± 0.98 \( \mu g/ml \) (\( p<0.05 \)); and 28.03 ± 2.40 \( \mu g/ml.hr \) to 56.51 ± 0.16 \( \mu g/ml.hr \) (\( p<0.05 \)) and 1.048 ± 0.02 hr⁻¹ to 2.781 ± 0.11 hr⁻¹ (\( p<0.05 \)) respectively. There was no change in the \( t_{\text{max}} \) (120.00 ± 0.43m) but there was a decrease in the \( k_{\text{el}} \) from 0.63 ± 0.20 hr⁻¹ to 0.46 ± 0.11 hr⁻¹ (\( p<0.05 \)). Similarly the \( C_{\text{max}} \), \( \text{AUC}_{0-4h} \) and \( K_{\text{a}} \) for hydroxy-ibuprofen rose from 43 ± 0.76 \( \mu g/ml \) to 45 ± 0.16 \( \mu g/ml \) (\( p<0.05 \)); 39.04 ± 2.30 \( \mu g/ml.hr \) to 59.49 ± 2.39 \( \mu g/ml.hr \) in (\( p<0.05 \)) and 1.498 ± 0.79 hr⁻¹ to 3.442 ± 0.23 hr⁻¹ (\( p<0.05 \)) respectively; while the \( C_{\text{max}} \), \( \text{AUC}_{0-6h} \) and \( K_{\text{a}} \) for carboxy-ibuprofen rose from 48 ± 0.71 \( \mu g/ml \) to 51 ± 0.16 \( \mu g/ml \) (\( p<0.05 \)); 41.97 ± 0.68 \( \mu g/ml.hr \) to 63.94 ± 0.12 \( \mu g/ml.hr \) (\( p<0.05 \)) and 1.649 ± 0.08 hr⁻¹ to 4.187 ± 0.42 hr⁻¹ (\( p<0.05 \)) respectively. The study has indicated that *Tamarindus indica* L. fruit extract significantly increased the bioavailability of Ibuprofen.

**INTRODUCTION**

Ibuprofen is one of the several phenylalkanoic acid derivatives that have anti inflammatory, analgesic and antipyretic actions and is used in the treatment of rheumatoid arthritis, osteoarthritis, alkylosing spondylitis and gout. Considerable interest has been shown in the possible effect of concurrent administration of traditional plant food drug materials with conventional pharmaceutical products. In developing countries, plant materials constitute the greater part of the dietary intake of the community. The plants are either consumed raw or prepared in a special way as soup or stew to form part of the daily meal. In addition to this, plant materials may be prepared in a form of traditional medicine for the treatment or cure of a wide variety of ailments and disease conditions. It is an established practice that these plant food drug materials are co-administered with conventional modern pharmaceutical products indirectly as part of the normal meal or directly as medicinal preparation. For example, *Tamarindus indica* L. fruit extract incorporated in a traditional food drink is commonly and habitually taken by the local people especially when recovering from illness or to stimulate appetite. Also this particular food drink is habitually taken by elderly people probably because of its...
sour taste. Also among the analgesics commonly and habitually taken by these elderly people is Ibuprofen. Many of these plant food materials contain pharmaco-active constituent, which may likely give rise to chemical or pharmaco-dynamic interactions with the conventional pharmaceutical products. The importance of these interactions to therapy is quite obvious. For example, the leafy part of many medicinal plant food materials such as Abrus precatorins, Hibiscus sabdariffa and Momordica charantia are rich sources of calcium. Co-administration of these plant preparations in the form of conventional meal or medicinal preparations with tetracycline would indeed have adverse clinical effects (1 - 3). Similarly, reduced clinical efficiency of penicillins has been reported following co-administration with fruits of Adansonia digitata, Psidium guajava and Tamarindus indica. (4).

The purpose of the present study was to evaluate the effect of the fruit extract of Tamarindus indica L. on the bioavailability of Ibuprofen. The fruit could be taken alone or mixed with other ingredients, like limejuices or honey, as a laxative and as a cold drink for patients with fever or dysentery. Of particular interest is its common use among the Hausas in the preparation of a pap or porridge from cereals served as part of breakfast or given to the sick to stimulate appetite. Its co-administration with Ibuprofen and other pharmaceutical products is a common practice among the local people.

**MATTERIALLS AND METHODS**

**MATERIALS**

All chemicals used, unless otherwise stated, were of analytical grade. T. indica fruits were purchased from the local market. Ibuprofen tablets were purchased from registered pharmaceutical chemist’s shop, while standard Ibuprofen powder was donated by Upjohn (Kalamazoo, MI, USA), hydroxy-Ibuprofen and carboxy-ibuprofen standard powders were donated by Kanoldt (Hochstadt/Donau, FRG). Flurbiprofen used as the internal standard was obtained from Eli lilly (Giessen, F.R.G.)

Waters 204 HPLC model equipped with 441 model U.V detector fitted with 254mm filter model U6k septumless injector and SE 120 model recorder was used. The column used for the chromatographic separation was a μ - Bondapak radial pak cartridge; polyethylene 15cm x 8.0mm I.D packed with 10μ m reversed phase C₁₈ support, waters part No. 85721 (water Associates Inc. Milford).

Also employed in the study were tablet dissolution and disintegration test apparatus (Erweka).

**METHODS**

Identification tests, dissolution and disintegration rate tests and assay for content of active ingredient in the ibuprofen tablets were carried out as per the BP 1993 specifications.

**Preparation of Standard Meal (Millet Porridge)**

50g of finely powdered millet grain (Penninsetum spp.) was placed in a clean bowl and about 40ml of water was added. The mixture was stirred with a spoon to produce a homogenous suspension. Boiled water (500ml) was added and stirred gradually to produce a relatively light porridge, which was further thickened by placing the bowl on a hot plate with constant stirring. The bowl was removed from the hot plate and allowed to cool. The pH of the mixture was 5.3.

**T. indica Water Extract**

Pieces of dried T. indica weighing about 50g were placed in a clean conical flask of a suitable size and 500ml of distilled water added enough to cover the pulp inside the flask and allowed to soak for 3 hours. The water extract, which was light brown in colour, pH 3.5, sour in taste and acidic to litmus paper was then decanted from the flask and filtered through a domestic sieve (100 mesh).

**Millet Porridge with T. indica Extract**

The same procedure for the preparation of the millet porridge was followed as described earlier. While the porridge was still hot, 100ml of the T. indica fruit extract was gradually added with stirring to produce a homogenous mixture. The porridge was further thickened by placing the bowl on the hot plate for about 10 minutes with constant stirring. The final pH of the mixture was 3.2.

**IN VIVO STUDY**

Six healthy male volunteers participated in the study. The average age and weight of the volunteers were 22.3 years and 66.4kg respectively. The volunteers were clinically certified fit for the study and were asked to refrain from taking any drug for at least 2 weeks before the commencement of the study. They were all non-smokers and did not take alcohol. A wash out period of 2 weeks trial was adopted.

The first stage of the study involved the ingestion of a 400mg dose of Ibuprofen tablets with about 100ml water after overnight fasting. Food was withheld for another 2hrs