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SHORT COMMUNICATION

Studies on *Bridelia ferruginea* Leaves (1). Stability and Hypoglycaemic Actions of the Leaf Extract Tablets

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The flavonoid content of 187.5 mg of *Bridelia ferruginea* leaf extract was calculated to be approximately 0.015% based on rutin. There was no significant difference ($p = 0.05$) in the mean values of flavonoids for the tabletted and untabletted extract. The moisture adsorption of the crude drug tablets was of Vander Waals type. The tablets showed a very long shelf life of about 96 years. A 25 mg/kg of *B. ferruginea* tablet lowered the blood glucose level of normal healthy rabbits by about 40%.

Keywords: Bridelia; tablet; stability; hypoglycaemic action.

INTRODUCTION

A method of analytical control of formulation of active ingredients of herbal products should be established since crude drugs formulations have been seriously criticized for their lack of dosage precision and standardization.

A crude drug that has been used in the treatment of diabetes mellitus is obtained from the plant *Bridelia ferruginea*. The leaf extracts have been reported to lower fasting blood sugar levels of maturity onset diabetic patients even in the presence of ketosis (Iwu, 1980). Addae-Mensah and Munenge (1986) have also shown that both pure rutin and the flavonoid mixture from the aqueous methanol extract of the leaves lowered blood sugar of fasting rabbits by about 35%. The mixture was found to contain about 75% of rutin and 25% of other flavonoids including quercetrin, quercetin-3-glucoside and myricetin-3-rhamnoside. They also reported that a daily dose of rutin up to 2.25 g for 7 days produced no toxic effects, indicative of an extremely low toxicity.

The present study was aimed at formulating the plant into a tablet dosage form, evaluating the stability and pharmacological activity of the crude drug formulation.

MATERIALS AND METHODS

The following materials were used: chloroform, glucose, sodium chloride, potassium acetate, sodium carbonate, aluminium chloride, sodium bromide, maize starch, lactose (M & B, UK); rutin, povidone (Merck, West Germany); Ac-Di-Sol, sodium adetate, trichloroacetic acid, benzoic acid, methanol, O-toluidine (BDH, Switzerland) and glibenclamide (Hoechst, UK).

The leaves of the plant (identified as *Bridelia ferruginea*) were collected in the month of May. The identity of the plant was confirmed by Mr A. Ozioko of Botany Department, University of Nigeria, Nsukka. Voucher specimens are deposited in the Department of Botany (herbarium section), University of Nigeria, Nsukka.

Preparation of *B. ferruginea* extracts. The leaves were dried at 50°C for 48 h. Size reduction was performed on the dried leaves using a hammer mill (Manesty, Liverpool) fitted with a 2 mm sieve. A modification of Humfreys method (Taha *et al.*, 1983) was employed for the extraction, using methanol/water (1:9) as the extracting solvent mixture.

Assay of rutin. A 0.1% stock solution of rutin prepared using methanol/water (1:9) solution was serially diluted to yield a concentration range of between 0.05%–0.005% for the preparation of a Beers plot.

Assay of *B. ferruginea*. A sample of the starch: drug mixture (562.5 mg) containing 187.5 mg of the dry leaf extract was introduced into a separatory funnel. A 30 mL solution of methanol/water (1:9) was added, and agitated for 2 min. This was extracted twice with 30 mL chloroform in a separatory funnel. The chloroform fraction was discarded. A freshly prepared 5% $AlCl_3$ solution was used to develop a yellow coloration. The absorbance was read at 405 nm, using as blank an aliquot of the purified extract stock solution. The assay was repeated five times and the average result determined.

Preparation of *B. ferruginea tablets*. The dried leaf extract/starch mixture was blended with pre-gelatinized starch in a 1:2 ratio. The resulting powder blend was mixed with Ac-Di-Sol and then wet granulated. Microcrystalline cellulose (5% w/w) was used as the binder. The lubricated granules were compressed in an F_3 single punch tabletting machine (Manesty, Liverpool), fitted with a 12.5 mm punch, at a tablet target weight of 700 mg.

Assay for tablet content uniformity. Twenty tablets were crushed to a fine powder. A 700 mg sample of the powder (equivalent to the weight of one tablet) was transferred to a

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clean separatory funnel. The assay procedure described earlier for *B. ferruginea* leaf extract was then adopted. The determination was repeated five times and the average value calculated.

Moisture content, moisture sorption and stability determinations were performed using standard methods (Ally, 1985). Mean values were expressed as % ±SEM.

Oral hypoglycaemic activity test. The O-toluidine method (Bauer *et al.*, 1974) was used to determine the glucose blood level. Glibenclamide was employed as a standard hypoglycaemic drug for comparison.

The mean blood sugar levels were expressed as mg %±SEM. The Students *t*-test was used to test the significance of difference between the treated groups and the control with $p=0.05$.

RESULTS AND DISCUSSION

The flavonoid content of 187.5 mg *B. ferruginea* leaf extract was estimated based on rutin. It was calculated to be 0.015% of the leaf extract. There was no significant difference ($p=0.05$) in the mean values of flavonoids in the tabletted and untabletted crude drug. This may well suggest that the stability of the active constituents in the formulation were not adversely affected by other formulation excipients and processing conditions.

The moisture content of the crude drug was reduced by about 4.3% when compressed into a tablet dosage form producing 5.82%±0.2%. This added quality might perhaps illustrate the advantage of tablet dosage form in enhancing the stability of potent drugs. The moisture adsorption pattern of the *B. ferruginea* tablets showed a Vander Waals type moisture adsorption, since the amount of adsorbed moisture was a function of the vapour pressure of the water molecules. This phenomenon may be explained by the simplified Langmuirs adsorption equation which has been made to assume a form in which the amount of moisture adsorbed is directly proportional to the vapour pressure of the gas (Nickalsson and Nyquist, 1983).

A plot of log concentration of *B. ferruginea* tablets against time of degradation revealed a first order degradation mechanism. Arrhenius equation was applied to this plot because it enables predictions to be made that are based on accelerated data and shows a quantitative relationship between the specific reaction rate (K) and temperature (T) (Carstensen, 1974). A plot (Fig. 1), of log K against $1/_T$ produced a straight line (by regression) which was extrapolated to obtain K at room temperature. K_{25} is generally used to obtain a measure of the stability of drugs under ordinary shelf conditions at room temperature. K_{25} was estimated to be approximately 0.0011 while the shelf life of the crude formulation was calculated to be about 96 years, indicative of a very high stability. This very long shelf life may reasonably be attributed to the high stability of the flavonoidal constituents of the crude drug at high temperature conditions.

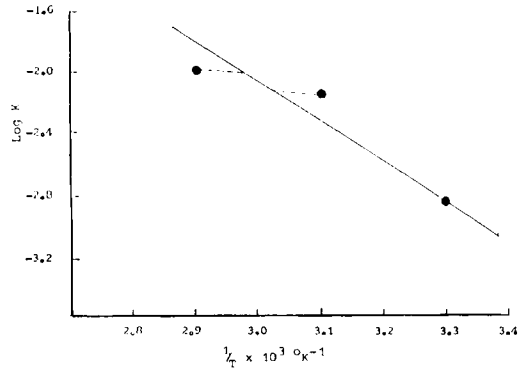

Figure 1. The Arrhenius plot of temperature (°K) and degradation constant (K) of flavonoids in *B. ferruginea* tablets.

The result of *B. ferruginea* leaf extract tablets on the blood glucose level of rabbits is presented in Fig. 2. The results show that the tabletted leaf extract evinced a dose related lowering of blood glucose similar to that of glibenclamide. A maximum reduction in blood glucose occurred within 2 h. The observation agrees with the results of Addae-Mensah and Munenge (1986), who recorded a time of about 90 min for the attainment of maximum reduction. However, glibenclamide demonstrated a higher potency and a longer duration of action than *B. ferruginea* leaf extract on a milligram per milligram basis.

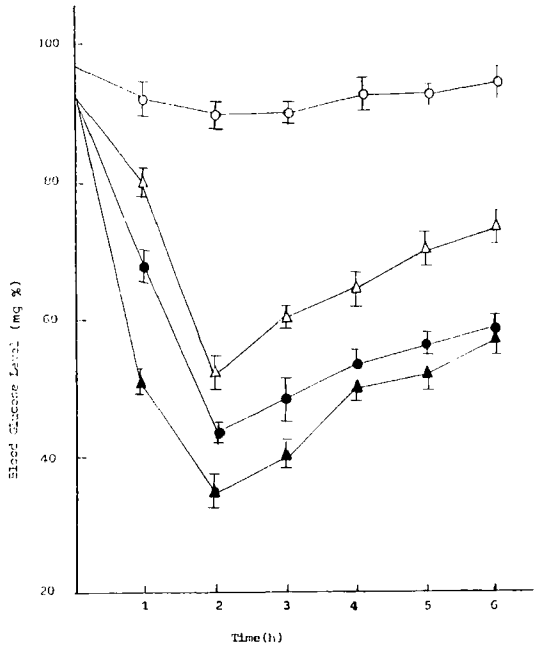

Figure 2. Variations in blood glucose levels of rabbits dosed with: ▲ 75 mg/kg *B. ferruginea*; ● 2.5 mg/kg glibenclamide; △ 25 mg/kg *B. ferruginea* and ○ 2 mL/kg of distilled water. Each point is the mean of 4 determinations ±SEM.

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