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GC Determination of parthenolide in feverfew products

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Feverfew (*Tanacetum parthenium* L., Asteraceae) has recently reemerged as a migraine prophylactic herbal product in Europe and in North America [1]. The major chemical constituent of feverfew is the sesquiterpene lactone parthenolide, and it is believed to act in migraine prophylaxis via inhibition of serotonin release from blood platelets in addition to other mechanisms [2–4]. A number of randomized, double-blind, placebo-controlled clinical trials have been conducted on feverfew with the majority favoring feverfew over placebo [5]. Among the proposed references for establishing quality control of feverfew preparations are a minimum level of 0.1% or 0.2% parthenolide in dried leaves as adopted by the French Ministry of Health and by the Canadian Health Protection Branch, respectively [6]. Feverfew products from the Canadian and European markets have been simultaneously analyzed by HPLC, NMR and biological methods and all were consistent in showing a high variability of parthenolide content [3]. In a previous report, we applied a validated HPLC method to determine the levels of parthenolide in a number of feverfew products purchased in the United States [7]. Results indicated a high level of variation among these products and a marked deviation from the Canadian and French standards. In this report, a simple gas chromatographic method coupled with flame ionization detection is introduced as an alternative to the HPLC method reported earlier. Compared to our previously reported HPLC method, the present GC method employed the same sample preparation procedure, had comparable sensitivity in detecting parthenolide and the analytical run time was almost the same. Representative GC chromatograms for standard parthenolide and for an analyzed sample are shown in Fig. 1. As shown in Fig. 2, both methods reflected the wide variation in the amounts of parthenolide in the different products obtained from the US market. Meanwhile, there was a close correlation between the levels of parthenolide obtained by both methods indicating comparable accuracy.

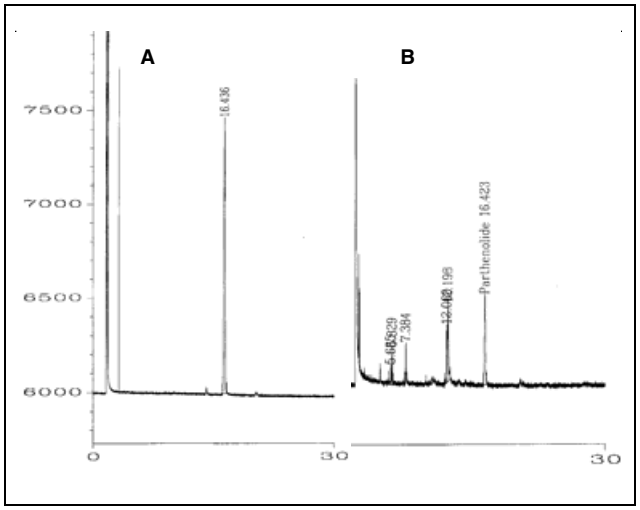

Fig. 1: Gas chromatograms of (A) standard parthenolide; and (B) feverfew sample B

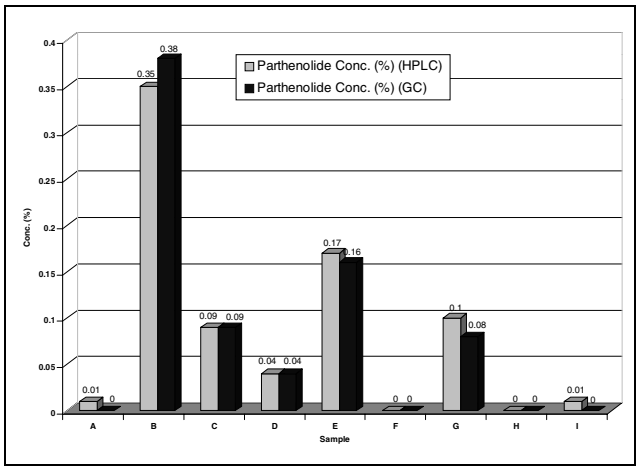

Fig. 2: Parthenolide levels (%, w/w) in analyzed feverfew samples

The method described in this report can be applied as an alternative to the HPLC method reported earlier. Either method is suitable for determining parthenolide levels in feverfew preparations to make sure that they comply with quality control standards adopted in different countries.

Experimental

1. Materials and instruments

Selected feverfew preparations were purchased through the internet from www.nutrimart.com. Parthenolide standard was purchased from Aldrich (St. Louis, MO). All solvents were of analytical grade. A Hewlett-Packard model 5890 gas chromatograph equipped with an auto-injector, flame-inonization detector (FID) and a PC running HP Chemstation software under Microsoft Windows 3.1 was used.

2. Sample preparation

Dry samples (capsules, tablets) were exhaustively extracted as follows: 100 mg of powder was sonicated in 3 ml of CH_3CN for 10 min in a Falcon® tube, the tube was centrifuged for 5 min and the supernatant transferred to a 10 ml volumetric flask. This was repeated twice and the final volume of the extract was adjusted to 10 ml with CH_3CN. An adequate volume was passed through a membrane filter (0.45 μm) into the appropriate sample vial and directly injected on the GC (5 μl) column.

3. GC analysis

A DB-1 (minibore, 20 m × 0.18 mm) capillary column was used at an isothermal column temperature of 200 °C for 30 min. The carrier gas was helium (45 psi) at a flow rate of 0.5 ml/min, and a split ratio of 50 : 1. Quantification was based on a five-point calibration curve derived from a concentration range of 25 μg/ml to 400 μg/ml for parthenolide ($y = 36.8x + 139$, $R^2 = 0.997$).

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Comparison of penetration rates of magnesium through the rat ileum for selected organic salts

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Magnesium is necessary for growth and many basic functions of living organisms [1, 2]. The deficiency of magnesium in humans could be treated by a proper diet or medication [3–5]. Many magnesium preparations are administered prophylactically as well as for curative purposes in magnesium deficiency [4, 5]. The absorption rates of magnesium are relatively low: only 30–40% of the dose are absorbed in the ileum [6, 7]. Usually, magnesium in preparations contain inorganic compounds e.g.: chloride, oxide, carbonate, sulphate or organic salts e.g., asparaginate, lactate, gluconate, citrate, and ascorbate.

Fumarates of selected elements were applied for therapeutical purposes, e.g., ferrous fumarate in anemias caused by a deficiency of iron. The ferrous fumarate was characterised by the lowest toxicity and a high bioavailability among the studied iron preparations [8, 9]. Magnesium fumarate has a magnesium content higher then magnesium gluconate (ca. 17.6% vs. 5.9%). The mentioned salt rejoins curative properties of magnesium and fumaric acid [10]. Up to now, no wide use of magnesium fumarate in supplementation therapy is reported in the accessible literature.

The intention of our study was to compare *in vitro* the penetration rates of magnesium available from the organic magnesium salts: fumarate and gluconate and the inorganic magnesium chloride. An apparatus containing a segment of reversed rat's ileum introduced into the circulating 0.9% sodium chloride aqueous solution was used for measuring the penetration rate of magnesium through the ileum.

The penetration rates of magnesium in %, determined for the studied solutions containing various magnesium concentrations after two hours of the experiment time are presented in the Table. The higher absorption rate of magnesium was observed for the fumarate solutions in comparison to the gluconate and chloride solution. Differences between the penetration rates of magnesium gluconate and fumarate were statistically significant ($p < 0.05$) in comparison to magnesium chloride. The penetration process of magnesium had higher velocity at the beginning of the experiment. The total quantity of magnesium absorbed decreased with a decrease in the concentration difference of magnesium in the two liquids used in the *in vitro* system: the stationary liquid containing magnesium salt and the eluent. According to published data [11, 12], a higher bioavailability and a lower toxicity were observed for the organic magnesium compounds. Szyszka *et al.* [12] assumed that no preference for any of the studied magnesium salt was observed. Preparations of magnesium characterised by an increased availability and low side effects could be very appreciated. In such cases the therapeutic dose might be decreased considerably. Magnesium fumarate fulfills these demands and could be introduced for magnesium deficiency therapy in humans.

The results of the magnesium absorption measurements carried out *in vitro* indicated that the absorption rate from magnesium fumarate solution is 5.4% higher than from the magnesium gluconate, and 17.3% higher than from magnesium chloride solutions. In the studied concentration range no influence of the magnesium dose on the absorption rate was observed.