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HPLC determination of caffeine in a multicomponent preparation

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Nutraceuticals (Functional foods, Pharmafoods), are a group of commercial products which stand in an growing interest of pharmacists; nutraceuticals play a very important role in practical pharmacy [1, 2].

Caffeine is a very frequent component of nutraceuticals. It is similar to alcohol and nicotine, a socially tolerated toxic substance, but in sports its use is very strongly limited. Therefore, the exact amount of caffeine in nutraceuticals should be known. A large variety of HPLC methods have been described for the determination of caffeine in pharmaceutical preparations [3–6]. The procedure is usually very simple because of the limited number of other compounds presented in the formulation. More complications occur when caffeine is presented in more complex multicomponent preparations containing vitamins, aminoacids and plant extracts, common components of many nutraceuticals.

The aim of this study was to develop a simple, rapid and accurate method for analysis of caffeine in a multicomponent preparation (Carnitol® plus). One ampoule (22 ml) contains: L-Carnithine 1000 mg, L-arginine 1000 mg, extract of *Guarana* 1000 mg, L-ornithine 500 mg, ascorbic acid 180 mg, myo-inositol 500 mg, α-tocopherol 50 μg, β-caroten 50 μg, selenium 25 μg *(organic bound)*, extract of *Garcinia* 250 mg, chromium-picolinate 400 μg and peptide FM 100 mg. The amount of caffeine is not declared, but relatively high concentration occurs in extract of *Guarana*.

The UV spectrum of a caffeine solution (6 μg/ml) showed two absorption maximum one at 206 nm and at 273 nm. Because of the better selectivity in higher wavelengths, all analyses were done at 273 nm.

A HPLC procedure described by Waters [6] was optimised (composition of mobile phase, pH, flow rate, separation column and sample preparation). Quantification of caffeine was based on the least-squares linear regression analysis. The calibration curve displayed very good linearity over the range 20–120 μg/ml for caffeine. The linear regression was:

$y = 0.21916\ (\pm 0.00107) \cdot x + 0.00548\ (\pm 0.00417)$; $r^2 = 0.99995$

This showed that the described mobile phase and chromatographic conditions, for linearity and sensitivity, were sufficient for a selective elution of caffeine.

The chromatographic method also provided satisfactory precision and accuracy. The relative standard deviations (R.S.D.) were always less than 2%. Under the chromatographic conditions used, caffeine and the internal standard paracetamol gave sharp and symmetrical peaks with retention times of 4.1 and 6.7 min, respectively.

The limit of quantification as the lowest standard concentration which could be determined with acceptable accuracy and precision (the R.S.D. was less than 1,2%) was 20 ng/ml.

Experimental

1. Chemicals and reagents

Pure samples of caffeine and paracetamol (IS) were purchased from SIGMA (St. Louis, Missouri, USA), acetonitril*e* (isocratic grade) and methanol

were obtained from Merck (Darmstadt, Germany), ammonium acetate was obtained from Balex (Pardubice, Czech Republic), acetic acid from Lachema (Neratovice, Czech Republic), water was purified by Osmium™ and Elix™ system (Millipore Corporation, MA, USA). All reagents used were of analytical-reagent grade.

2. Chromatography conditions

The HPLC consisted of an isocratic pump HPP 5001 (Laboratory Instruments, Prague, Czech Republic), a detector Waters™ 486 and data module Waters 746 (Waters Corporation, Milford, MA, USA), a LCI 30 injection valve (ECOM, Prague, Czech Republic) with a 10 µl loop. Analyses were performed on a column 5 µm SGX C18 (150 × 3mm I.D., Tessek, Prague, Czech Republic). The optimal mobile phase was a mixture of acetonitril/20 mM ammonium acetate, pH = 5.5 (20 : 80). The flow rate was set at 0.5 ml/min. The UV absorbance was monitored at 273 nm.

3. Preparation of standard solutions

Stock standard solution of caffeine and paracetamol (IS) were prepared in methanol by dilution of 0.2 mg/ml and 28 mg/ml, respectively. Calibration standards were prepared by volumes of stock standards solution of caffeine and IS (concentration range 20–120 µg/ml for caffeine).

4. Sample preparation

One ml of the pharmaceutical preparation was pipeted into a 50 ml volumetric flask, 1ml of solution of IS was added and diluted to the mark with methanol. The sample was placed in an ultrasonic bath for 5 min and after sonication was filtered with SPARTAN 30/B 0.45 µm.

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Measurement of film thickness on the surface of coated pellets and its influence on drug dissolution rate

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Film-coated solid dosage forms, e.g. pellets and tablets, are currently of increasing importance. An appropriate coating fluid applied to a pellet surface produces a macromolecular film coat, the properties of which will influence the pellet parameters and the liberation of drug from the pellets and from the tablets manufactured from them [1–5].

The thickness of this film influences the kinetics of dissolution of the drug. For this reason, characterization of such a film is of great importance. Such measurements are very easy in the case of tablets. It is possible to measure the geometrical parameters of the tablets with a screw micrometer before and after the coating process. Application of this method is not possible in the case of pellets because of the smallness of the particles [6]. Therefore, the aim of the present work was to investigate another method for thickness measurement and the influence on the drug dissolution rate.

An image analysis method was used to determine the thickness of the coating films. Before the determination, a sieved range of pellets (0.63–0.75 mm) was selected. This separated fraction was coated. The diameters of the pellets were measured before and after coating. Three series of coated pellets were prepared. Each series consisted of three batches and the same mass of pellet core (200 g) was used in each batch. In the first group of batches, 100 g of different coating dispersion was sprayed onto the pellet core. In the second group of batches, 200 g of coating dispersion was used. In the third group of batches, 300 g of coating dispersion was sprayed onto the pellet core. Finally, 400 g of coating dispersion was used. The dry material content of the dispersions was different. The results of the film thickness measurements are presented in Fig. 1.

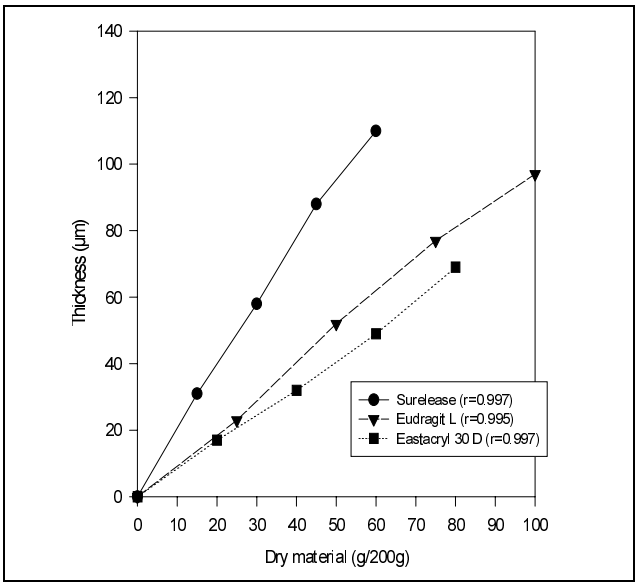

Fig. 1: Relationship between film thickness and dry material content of coating dispersion