

Poster Session 2 – Analytical Chemistry

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Qualitative and quantitative determination of active components of *Matricaria recutita* L. oil extracts

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Flowers of *Matricaria recutita* (FMR) are used in medicine as an anti-inflammatory, spasmolytic and antiseptic remedy. The composition of FMR extracts by polar solvents is well investigated. They contain flavonoids, coumarins, precursors of chamazulene, etc. However, the possibility of the creation of new medicinal forms based on FMR is not yet exhausted. Hydrophobic extragents are used for preparation of FMR lipophilic complexes such as plant fixed oils enriched by more hydrophobic components. For characterization of these objects it necessary to identify and quantify their biologically active compounds (BAC). The goal of the present work is determination of the content of volatile and non-volatile extractive compounds in FMR oil extracts.

The samples of oil extract of FMR were prepared with use of a rotopulsed extractor by original technology. Soya and olive oils were used as extragents. The analyses of individual non-volatile compounds have been carried out on LC-chromatograph with UV-detector (wavelength 320 nm) on the reversed-phase column C_{18}. The major component, isolated by preparative HPLC and characterized by mass spectra, was identified as 3,5,6-trihydroxy-4,6-di(3-methyl-2-butenyl)-2-propionyl-2,4-cyclohexadien-1-one ($C_{19}H_{26}O_5$, MW 334, trivial name posthumulone). The constituents of the volatile fraction of FMR oil extracts were identified by their mass-spectra and GC retention indices on standard non-polar phases Zenkevich (2002). The principal of them are (E)- and (Z)-2-[2,4-hexadiynyl]-1,6-dioxaspiro[4.4]-non-3-enes (en-yn-dicycloether 1 and 2, correspondingly) (Hyvonen et al 1991). The content of some compounds in FRM soya oil extracts on results of five series are presented in Table 1.

Table 1 Content of some volatile and non-volatile individual components of *Matricaria recutita* soya oil extracts

	Content (% × 10^3)
Non-volatile compounds	
Umbelliferon	1.1 ± 0.2
Herniarin	4.4 ± 0.5
Apigenin	0.6 ± 0.2
Isoposthumulone	10 ± 1.0
Posthumulone	52 ± 3.0
Volatile compounds	
α-Bisabololoxide B	>1.6
Chamazulene	0.18–10.5
En-yn-dicycloether 1	7.9 ± 1.3
En-yn-dicyclother 2	3.4 ± 0.5

For the analyses of flavonoid's sum content in oil extracts of FMR differential UV-spectrophotometry with aluminium chloride as the reagent have been used. Its value determined with quercetin as reference substance in oil extracts of FMR was 0.0030–0.0045% w/w.

The using of HPLC, MS, GC-MS and UV-spectrophometry allows us to determine the principal groups of BAC in oil extracts of FMR. Posthumulone and isoposthumulone prevail over other compounds in oil extracts of FMR. Their presence has never been reported previously for *Matricaria*. Obtained data are useful for creation and standardization of new preparations from FMR oil extracts.

Zenkevich, I. G. (2002) Abstr. of 25th ISCC. Italy, Rep. A10 (CD-ROM)
Hyvonen, H., et al (1991) *Acta Pharm. Fenn.* **100**: 269–273

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Mapping and characterisation of the components of a model paracetamol tablet with scanning thermal microscopy

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Solid dosage forms such as tablets or pellets commonly include a mixture of excipients and active ingredient. In many circumstances the distribution of the different components throughout the formulation will have a significant effect on the product's performance. Consequently methods that can spatially characterise such systems are of great interest. One example is Scanning Thermal Microscopy (SThM), a novel imaging technique developed from AFM. SThM generates lateral maps of thermal conductivity that often reveal surface heterogeneity. Furthermore, localised thermal analysis is possible, enabling identification of the components located by thermal imaging. Despite the obvious potential of this technique for pharmaceutical characterisation, few applications have been reported.

In this study, compressed tablets containing micronised paracetamol and lactose monohydrate (50:50 by weight) were analysed using a Thermomicroscopes SThM instrument. SThM operates in contact mode, where thermal conductivity maps are obtained by recording the power required to maintain the tip at a constant temperature. Measuring the deflection of the static cantilever as a temperature ramp applied to the tip performs localised thermal analysis.

Thermal imaging of the tablet surface reveals elongated low thermal conductivity domains within a higher conductivity matrix. It is well known that changes in tip-sample contact area due to sample topography can contribute to thermal contrast. To assess this effect, a blind reconstruction method was employed to determine the thermal probe tip shape. This resulted in an estimated tip radius of 590 nm. Using this tip radius, a certainty map was produced, which indicates regions in which constant tip apex-sample contact occurs. This map revealed that the observed thermal contrast was not solely induced by the sample topography. This novel verification method proves that the heterogeneous composition of the tablet has been detected using thermal imaging.

Localised thermal analysis allows the material producing the thermal contrast to be uniquely identified, and reveals that the low conductivity domains are composed of paracetamol (m.p = 168–170°C), while the surrounding regions consist of lactose monohydrate. Interestingly, the melting point for the lactose domains determined using SThM was 195 ± 5°C, lower than the reported melting point of lactose monohydrate (214°C). This is explained by the presence of an endothermic thermal event at 120°C in the SThM trace. It is likely that this peak indicates dehydration of lactose monohydrate to the anhydrous form. Anhydrous lactose has a lower melting point (200–202°C), in good agreement with the SThM data. Further evidence is provided by the morphology of the domains, which agrees well with previous AFM topographical images of micronised paracetamol that depicted similar elongated crystals.

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HighSpeed differential scanning calorimetry of polymorphic transitions in nifedipine

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Previously, Eckert & Müller (1977), Keymolen et al (2002) and Hirayama et al (1994) reported the appearance of several events in the DSC scans of glassy nifedipine obtained at slow heating rates. These were attributed to the presence of

Form I (melting peak at 172°C), Form II (melting at ~163°C) and Form III (melting at ~135°C) polymorphs. In this study, the behaviour of glassy nifedipine was investigated using a novel technique, HighSpeed differential scanning calorimetry. The chemical stability of nifedipine during DSC has been previously established (Keymolen et al 2002).

In this study, nifedipine BP was used with a sample mass of 0.6 ± 0.05 mg enclosed in standard crimped aluminium sample pans. A PerkinElmer Pyris Diamond Power Compensation DSC coupled to an Intracooler 2p was employed. Scan programs involved heating from 30° to 200°C at 50°C min^{-1}, cooling from 200° to 0°C at 200°C min^{-1} and an isothermal hold for 2 min at 0°C. The glassy samples were subsequently scanned from 0° to 180°C at 10°, 20°, 50°, 75°, 100°, 125°, 150°, 200°, 250° or 300°C min^{-1}. Nitrogen (30 mL min^{-1}) was used as purge gas.

At 10°C min^{-1} the nifedipine exhibited a number of recrystallisation events in the range 95–110°C. These events have been confirmed previously by optical microscopy (Keymolen et al, 2002). The phase transitions from Form III to Form II and from Form II to Form I were both easily observed at this scan rate. At the higher scan rates, nifedipine was given insufficient time to recrystallise to Form III and so the multiple recrystallisation processes and transition of Form III to Form II were lost. With increasing scan rate, there was also a change in the ratio of Form I to Form II formed during the recrystallisation: the relative amount of Form I increased with increase in scan rate. Additionally, the glass transition of nifedipine became increasingly apparent with increase in scan rate.

The polymorphic transitions exhibited by nifedipine were dependent on the scan rate. HighSpeed DSC potentially allows the study of materials that exhibit polymorphism as a function of the scan rate without the occurrence of the polymorphic changes during the scanning process itself. The accelerated scan rate therefore gives a snapshot of the sample as manufactured without subsequent phase changes induced by slow sample scanning. The use of fast scanning rates (up to 300°C min^{-1}) and small sample size (< 1 mg) of glassy nifedipine samples revealed the dependence of the polymorphic transformations occurring prior to the main melting endotherm, at 172°C, on the heating rate.

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Hirayama, F., Wang, Z., Uekama, K. (1994), *Pharm. Res.* **11**: 1766–1770
Keymolen, B., Ford, J. L., Powell, M., et al (2002) *Thermochim. Acta* In press