## Session No. 3
## The formulation of a plant based drug – technological, analytical and biopharmaceutical issues

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*Wirginia Kukuła-Koch, PhD habilitated in pharmaceutical sciences, university professor*
*Professor Małgorzata Sznitowska, PhD habilitated in pharmaceutical sciences*
*Professor Marian Mikołaj Zgoda, PhD habilitated in pharmaceutical sciences*

**7. Peruvian maca (Lepidium peruvianum) – current application possibilities based on own studies**
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**8. Cannabis flos and Cannabis floris extractum normatum – raw materials for medicinal products compounded by pharmacists in Poland and other countries**
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**9. Pharmaceutical availability (Q%) of phytochemicals from Linden Flower Extract (Tiliae flos ext.) in receptor fluids after disintegration of the model solid uncoated drug form**
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## 7. Peruvian maca (Lepidium peruvianum) – current application possibilities based on own studies

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### Introduction:

Peruvian maca (*Lepidium peruvianum* syn. *Lepidium meyennii*) from the Cruciferous family is obtained for pharmaceutical purposes from Andean plantations, where it is grown at an altitude of over 3000 m above sea level. Due to its immunotropic and strengthening properties, this plant is called a Peruvian ginseng.

This report aims to present the recent studies on the inhibitory activity of maca extracts towards two enzymes: acetyl- (AChE) and butyrylcholinesterase (BuChE). These properties are of key importance in regulating the memory process in the elderly patients with memory deficits. In addition, information on the bioavailability of individual metabolites from the extracts in the digestive process will be presented.

**Material and methods**: Extracts of maca tubers of different colors obtained from two plantations of Junin and Ankash in Peru were subjected to composition analysis using the HPLC-ESI-QTOF-MS/MS technique and assays for the inhibitory activity against two cholinesterases in a modified Ellmann's test. The total extracts were also digested in an artificial gastrointestinal tract to check the effect of digestive enzymes on the stability of the metabolites. Also, the affinity of glucosinolates to both enzymes was tested.

**Results**: Peruvian maca extracts are sources of lepidilins, macamides and glucosinolates. It was confirmed that the latter inhibit the activity of AChE and BuChE, which may be important in the context of the potential administration of the plant in neurodegenerative diseases. Glucosinolates in the gastrointestinal tract were stable.

**Conclusions**: Lepidium peruvianum is a source of metabolites that can be used for procognitive studies.

## 8. Cannabis flos and Cannabis floris extractum normatum – raw materials for medicinal products compounded by pharmacists in Poland and other countries

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Medical marijuana can be used in clinical practice in Poland on the basis of the Act from July 7, 2017, amending two other acts: the act on counteracting drug addiction and the act on reimbursement of drugs, foodstuffs for particular nutritional uses and medical devices. Only the substance (herbal substance, i.e. cannabis inflorescence - Cannabis flos or its preparations), which is the raw material for the preparation of a prescription drug, may be authorized. This means that a pharmacist has to process such a raw material and can dispense it on the basis of a prescription for a compounded medicine, issued for an individual patient.

In practice, from Polish pharmacies usually unprocessed inflorescence is delivered, very often in the original packaging, without dispensing as individual doses. There are no standard procedures for preparation of the material if it is intended for vaporization. Both the medical and pharmaceutical communities are waiting for a formulary containing guidelines on the dosage of medical marijuana in drug forms such as capsules, ointments, suppositories and eye drops. Such various forms of the pharmacy compounded medicines may be prepared using a standardized extract with a defined decarboxylated cannabinoids content.

Many countries have officially established institutes or agencies dealing with the standards of treatment and the quality of cannabis products under the auspices of, or working closely with, the ministry of health. Canada, the Netherlands, Israel, Germany and Italy seem to be the world leaders in terms of such properly prepared guidelines. Unfortunately, there is no such government initiative in Poland.

## 9. Pharmaceutical availability (Q%) of phytochemicals from Linden Flower Extract (Tiliae flos ext.) in receptor fluids after disintegration of the model solid uncoated drug form

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Estimation of the physicochemical properties, and most of all the actual solubility (-log $x_2$) and the level of hydrophilic-lipophilic balance ($HLB_{Requ.}$) of phytochemicals included in the linden flower extract (*Tiliae flos ext.*) prompted pre-formulation studies to develop a model solid oral form of drug of the "fast dissolving tablets"-type.

The model form of the preparation for pre-formulation studies was manufactured by the technique of direct tableting with one excipient of specific granulometric structure and homogeneous grain size (Vivapur 105, Vivapur 112, Vivapur 200, Prosolv SMCC 50, Prosolv Easy tab. SP., EMDEX).

The morphological parameters and the effective time of tablet disintegration were determined, and first of all, the pharmaceutical availability (Q%) of phytochemicals in model receptor fluids (in water and 0.1 mol HCl) was tested in a function of time (t, min).

Using mathematical models such as: Q%=f(t), Q%=f($\sqrt{t}$), and $\sqrt[3]{100}$-$Q_t$=f(t), the course of the relationship between pharmaceutical availability (Q%) and exposure time (t, min) in model receptor fluids was described with approximation equations at p=0.05.

Using the coefficients of the approximation equations log y=a+b·x and the dependence

$$P_{c.u}= \int_{t_1}^{t_2}( a + b \cdot x)dx = ax + \frac{bx^2}{2} \int_{t_1}^{t_2} dx$$

brought to the application version

$$P_{c.u}=t_2 \cdot a+\frac{b}{2}(t_2)^2 - [t_1 \cdot a+\frac{b}{2}(t_1)^2]$$

variants of the areas under the pharmaceutical availability curves were calculated in conventional units $P_{c.u}$. The calculated numerical values of $P_{c.u.}$ in the environment of model receptor fluids allowed to select an optimal excipient for manufacturing a model preparation of the "fast dissolving tablets"- type with the expected pharmacokinetic parameters. The published research results have shown that the introduction of a micellar solubilizer to the tablet mass will reduce the adsorption capacity of excipients, and at the same time, through effective solubilization, it will increase the solubility of phytochemicals contained in *Tiliae flos ext.*.