CANEPHRON N IN TREATMENT OF URINARY TRACT INFECTIONS IN CHILDREN

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Infections of the urinary system (IUS) are one of the most common diseases in children with the average growth of annual incidence of 6.1%. It has been clinically proven that the advantage of Canephron N is the combination of anti-microbial, anti-inflammatory and diuretic effects, which is especially valuable in chronic processes in the urinary tract [*K.G. Naber, T.S. Perepanova 2012; M.V. Erman 2012; Kurt G. Naber, 2013*].

Catheterization of the bladder is a rather common procedure in medical practice. Short-term catheterization generally does not cause any complications. However, increase of duration of stay of the catheter in the body increases the risk of infection, the so-called catheter-associated infections (KAI; in English publications CAUTI — catheter-associated urinary tract infection).

To determine the degree of the bactericidal effects of Canephron N on the process of biofilm formation on the internal surface of the urinary catheter and establish a possibility of its use for the prevention of catheter-associated infections.

The cultures of *Escherichia coli* M17 were grown as biofilms on the internal surface of the 2-way standard latex (siliconized) Foley catheter (Unomedica). After co-incubation of the obtained biofilms with Canephron N, the degree of bactericidal effects of the drug products on the bacteria by inoculation using the Koch's method was determined. The effect of Canephron N on the ability of bacteria to form biofilms was determined by culturing bacteria in the presence of the drug product. The product used in the experiment was Canephron® N from Bionorica SE (Germany). The ultrastructural changes in the cells and biofilms were evaluated on transmission electron microscope JEM 100C (JEOL, Japan) at accelerating voltage of 100 kV by positive staining of 0.1% uranyl acetate aqueous solution and by ultrathin section method.

Incubation of biofilms of *E. coli* M17 in the presence of undiluted Canephron N solution after 5 hours resulted in a decrease of the number of viable cells by 7 orders of magnitude lower than that in the control. No viable cells were detected in 24 hours.

It had been found that in addition to inhibition of biofilm formation of growing bacterial cultures of *Escherichia coli* M17 on the surface of the catheter, Canephron N also destroys the biofilms that have already been formed by them, which significantly reduces the risk of ascending infection during prolonged catheterization.

PRELIMINARY STUDY OF CHEMICAL COMPOSITION AND DIPEPTIDYL PEPTIDASE IV INHIBITORY ACTIVITY OF VARIOUS EXTRACTS OF *LARIX SIBIRICA* IN VITRO

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In today's world, diabetes is a problem of all ages and all countries. Diabetes is ranked third among the direct causes of death. The insulinotropic hormone, glucagon-like peptide 1 (GLP-1), which has been proposed as a new treatment for type 2 diabetes, is metabolized extremely by dipeptidyl peptidase IV (DPP-4). Inhibitors of DPP-4 enhance the level of GLP-1, which have improved glucose tolerance and increased insulin secretion. The literature contains information about the inhibitory effect of extracts of some plants in the DPP-4 activity.

Larch is one of the most common tree species in Russia. The extracts of wood and bark *Larix sibirica* were tested in-vitro for DPP-4 inhibitory activity to understand the therapeutic activity of *L.sibirica* extracts for the treatment of non-insulin dependent diabetes mellitus.

The extracts from the bark were obtained by sequential exhaustive extraction with diethyl ether, isopropanol, cold water and hot water. Extracts from the sapwood and heartwood were obtained by exhaustive extraction with cold (25 °C) and hot (90 °C) water. Nitrogen-containing compounds (N-compounds) was determined by ninhydrin reaction, flavonoids — by reaction with $AlCl_3$ in rutin equivalent's; phenolic compounds — by the reaction of Folin-Ciocalteu. Total carbohydrates were measured using the phenol–sulfuric method.

DPP-4 activity in human plasma was assessed using the substrate Gly-L-Pro-p-nitroanilide. Under the action of DPP-4 formed Gly-L-Pro and a detectable product

Table 1. Phytochemical characteristic and DPP-4 inhibitory activity of extracts of *Larix sibirica* (%, Mean ± sd)

Extracts	N-compounds	Flavo-noids	Poly-phenols	Poly-sacharides	DPP-4 inhibition
Hot water extract from sapwood	0,20±0,01	0,37±0,02	1,60±0,01	15,4±0,4	20–30*
Cold water extract from sapwood	0,10±0,01	0,18±0,01	0,56±0,03	14,6±0,5	20–80**
Hot water extract from heart wood	0,10±0,01	0,57±0,03	0,97±0,04	12,4±0,3	n.i.***
Cold water extract from heart wood	0,12±0,02	0,97±0,04	1,67±0,03	8,4±0,2	n.i
Diethyl ether extract from bark	1,60±0,06	0,62±0,02	14,5±0,5	12,2±0,5	20–33*
Cold water extract from bark	2,11±0,08	1,93±0,08	21,3±0,6	23,0±0,7	12–65*
Hot water extract from bark	0,72±0,05	0,40±0,03	22,1±0,9	49±2	n.i.

* — concentration range 0,02–2,0 mg/ml; ** — concentration range 0,0002–0,02 mg/ml; *** — no inhibition.

p-Nitroaniline. In the presence of the DPP-4 inhibitor concentration decreases the reaction products [1]. Sitagliptin has been used as a standard inhibitor of DPP-4.

Table 1 contains phytochemical characterization of the active extracts. The concentrations of potential biologically active substances in the extracts of cortex are more than in wood, but the most potent inhibitor of the DPP-4 is an cold water extract from the sapwood.

Hot and cold water extracts from heart wood, hot water and isopropanol extracts from bark of L. sibirica don't inhibit the activity of the enzyme DPP-4. Cold water extract from bark in concentration 2 mg/ml inhibits the activity of DPP-4 to 65±7%, in concentration 0,02 mg/ml — to 12±2%. Hot water extract from sapwood at a concentration of 0,02–2,0 mg/ml to inhibits the action of DPP-4 in 20–30%. The most active inhibitors against DPP-IV are cold water extracts from sapwood of larch. The IC_{50} values of cool water extract from sapwood of larch was 0,11±0,02 μg/ml. This extract was more active than the 70% ethanol extract from the seeds of *Castanospermum australe* (IC_{50}=13,96 μg/ml) [2]. The IC_{50} value of sitagliptin for DPP 4 inhibitor was 25–32 nM (0,010–0,013 μg/ml) in human plasma.

The results confirm the inhibitory effect of cold water from sapwood on DPP-4, and the potential to be a novel, efficient and tolerable approach for the diabetes.

References:

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THE INVESTIGATION OF THE AGGLOMERATION AND ATTRITION PROCESSES OF THE GRANULES WITH ICELAND MOSS EXTRACT IN FLUID BED

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The investigation deals with the dry extracts obtained by extraction of Iceland moss (*Cetraria islandica*) with purified water, with subsequent spray drying. The dry extracts had high residual moisture and hygroscopicity, low flowability and compressibility, a large amount of dust fractions. The aim of the experiments was to study of agglomeration and attrition of the granules as the predominant processes during the granulation.

For the mathematical description of the agglomeration process can be used *Smoluchowski*'s kinetic equation, which for the purpose of this case takes the form (1):

$$\frac{\partial n(m)}{\partial \tau} = \frac{1}{2}\int_0^m \beta(m^\bullet, m - m^\bullet) \times n(m^\bullet) \times n(m - m^\bullet) dm^\bullet - \int_0^\infty \beta(m, m^\bullet) \times n(m) \times n(m^\bullet) dm^\bullet, \quad (1)$$

where τ is the process time, $n(m)$ is the number of particles in fluid bed, $\beta(m^\bullet, m-m^\bullet)$ is kernel of integral transformation that describes the probability of effective pair interaction of the particles with masses $m-m^\bullet$ and $m^\bullet$.

If we accept $\beta(m, m^\bullet)$ = const, than the average value of particle's mass depending on the time is determined by the equation (2):

$$m(\tau) = m_0\left[1 + \frac{N_0 B\tau}{2}\right], \quad (2)$$

where $B = \beta(m, m^\bullet)$ — coagulation constant, which characterizes the conditions of the agglomeration process and is determined by experimental data, N_0 is the number of particles at the initial time, m_0 is the average mass of the original particles, t is the process time.

The experimental study was carried out in a laboratory fluid bed apparatus ("AEROMATIC", type "STREA",