

leaves, to rats and understanding of the relevant mechanisms governing the intestinal absorption and pre-systemic elimination. To define the ginkgo compounds to be studied, literature informatics-guided chemical profiling revealed that GBE50 extract contained 72 ginkgo constituents, including terpene lactones, flavonols, flavones, an isoflavone, biflavones, flavanols, and carboxylic acids, at levels ranging from 0.01 to 55.3 mg/g. Among the ginkgo constituent groups were the terpene lactones and the flavonols that were significantly measurable in plasma after p. o. administration of GBE50 extract to rats. The intestinal absorption of terpene lactones appeared to be dictated by their intermediate membrane permeability, while the influences of MDR-1-and MRP-2-mediated intestinal efflux and the presystemic metabolism and biliary excretion might be relatively limited. Because of their deglycosylation

absent in the small intestine and relatively slow pre-systemic elimination, many intact flavonol glycosides appeared in the rat plasma albeit with a limited extent of absorption. Colonic deglycosylation of the flavonol glycosides occurred and the glucuronides of flavonol aglycones were also measured in the plasma. Although some biflavones also had relatively high abundance in GBE50 extract, these ginkgo constituents were not measured in the rat plasma because of their poor solubility and poor permeability that hindered the intestinal absorption. The levels of the remaining ginkgo constituents in GBE50 extract were too low to be measured in the rat plasma. The current study enabled us to better understand the nature of systemic exposure to ginkgo compounds after p. o. administration of GBE50 extract and to more precisely implement multicomponent PK study of the extract.

BIOPHARMACEUTICAL ASPECTS OF THE DEVELOPMENT OF A PHYTOECDISTEROIDS (PE) OINTMENT COMPOSITION

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PE are analogues of insect steroid hormones occurring in plants. The establishment of reparative activity of PE (1) makes it relevant to develop compositions on their base. PE molecules have six or more hydroxyl groups and hydrophobic core and therefore the influence of the ointment composition nature on the bioavailability of PE was trialed. In these investigations preparation *Serpisten* (mixture of 20-hydroxyecdison and 25S-inocosterone obtained from the plant *Serratula coronata* L.) has been used. For this purpose three types of compositions have been prepared at a concentration of *Serpisten* 0.02% (w/w): hydrophobic (lanolin and vaseline — C1), hydrophilic (3% sodium *carboxymethyl cellulose* gel — C2), emulsive (aerosil, vaseline oil, water purified, monoglyceride purified — C3). Biopharmaceutical evaluation of prepared formulations has been performed using drug releasing from the compositions by dialysis through a membrane with subsequent determination of the release profile in the UV region at $\lambda = 240\text{nm}$. The concentration of PE was determined at 30, 60 and 120 minutes of dialysis. The test revealed that the PE release from the C3 was al-

most entirely (100.2%), while from C2 76.5% of the total amount of PE was passed to aqueous medium, and from C1 only 37.5%. During the rheological studies it has been established that the shear stress at the C1 was less than 80 Pa*s at C2–300 Pa*s and at C3 156 Pa*s. C3 is the closest to the «*Bepanthen*» ointment (Bayer, Germany), which has the wound-healing activity (211 Pa*s.). For further PE reparative properties trials, C3 have been chosen, for this test linear aseptic wound model has been used. In five days it was found that, the scar strength in experimental group was 281.6 ± 40.4 gr., in control group 160.8 ± 18.0 gr. and in intact — 123.4 ± 20.0 gr. This data are higher 1.75 times in experimental group, compared with a control group ($p = 0.021$) and 2.28 times in the intact ($p = 0.009$). The result of this work was the development of preparing technology topical emulsive formulation having the high bioavailability.

Reference: (1) Meybeck A, Bont F. 1990. Ecdysteroid-containing liposomes for wound healing and skin regeneration. Demande FR 2,637,182. (*Chemical Abstracts* 114: 30138r).