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SOME BIOLOGICAL PROPERTIES OF TRITERPENOID ACIDS

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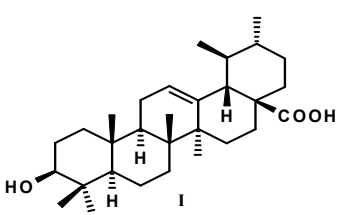
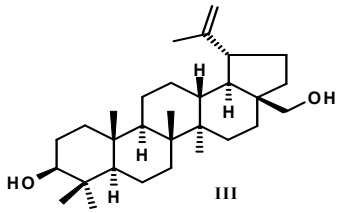
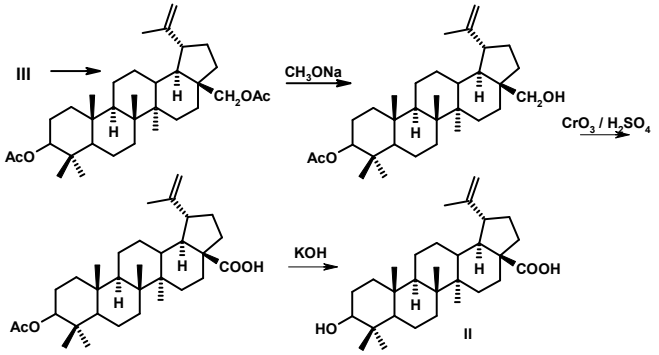
It is well-known that ursolic (**I**) and betulinic (**II**) acids, natural triterpenoids, possess wide spectrum of biological properties, including their ability to block the processes of angiogenesis [1-4], induce the apoptosis [5-9], thus they are of great interest for the treatment of oncological diseases.



I



III



II

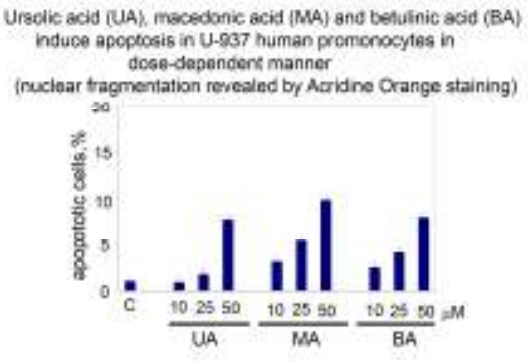
It is also known that anti-inflammatory action of betulinic acid is opposed by glucocorticoid receptors [10], therefore under the long-time application the risk of osteoporosis rises [11]. For the preliminary evaluation of this risk we have investigated the influence of these acids on some biochemical characteristics of ovariectomized rats using the modified model of Kalu. [12].

Ursolic acid (**I**) was separated from Uvae ursi, betulinic acid (**II**) was synthesized from betulin (**III**) (scheme). 17α-ethynylestradiol was a positive control. It turned out, that triterpenoid (**II**) does not have negative effect on mineral components in femur and possess cholesterol-lowering action under the experimental conditions, thus these compounds are perspective for the next investigations.

The influence of triterpenoids (**I**), (**II**) on the biochemical parameters of ovariectomized rats (Sprague Dawley line)

Group of experimental rats	Body weight change, g	Uterotropic action		Ash femur weight / Wet femur weight	Serum cholesterol, mg/dl	Serum triglycerides, mg/dl
		Uterine weight, mg/100 g of body weight	Progesteron receptors, fmol / mg of protein			
Sham-operated	30.6±2.7 **	156.7±8.9**	62±5**	0.440±0.006*	58.7 ± 1.8*	81.6±4.9*
Ovariectomized	65.5±4.2	34.5 ±2.6	18 ±2	0.396±0.005	70.7 ± 1.9	65.8±4.3
Ovariectomized, treated with EE, (0.1mg/kg)	9.0±4.1**	156.2 ±7.4**	102 ±11**	0.448±0.005*	27.2 ± 1.5*	122.7±12.6
Ovariectomized, treated with ursolic acid (**I**) (20 mg/kg)	62.5±4.1	32.4±3.5	20±2	0.385±0.008	46.3±2.2*	45.2±4.1*
Ovariectomized, treated with betulinic acid (**II**) (20 mg/kg)	64.1±5.3	29.8±2.5	22±3	0.407±0.005	49.4 ± 3.1*	57.3±5.1

The results of the influence of ursolic, betulinic and mecedonic acids on the apoptosis processes are presented in the Figure.



[1] Sohn K.H., Lee H.Y., Chung H.Y. et al. *Cancer Letters*, **1995**, *94*, 213. [2] Cadrenas C., Quesada A.R., Medina M.A. *Biochem. Biophys. Res. Comm.,* **2004**, *320*, 402. [3] Mukherjee R., Jaggi M., Rajendran P. et al. *Bioorg. Med. Chem. Lett.*, **2004**, *14***,** 3169. [4] Mukherjee R., Jaggi M., Rajendran P. et al. *Bioorg. Med. Chem. Lett.*, **2004**, *14***,** 2181. [5] Ya-Ling Hsua, Po-Lin Kuob, Chun-Ching Lina. *Life Sciences*, **2004**, *75*, 2303. [6] Cipak L., Grausova L., Miadokova E., Novotny L., Rauko P. *Archives of Toxicology*, **2006**, *80(7)*, 249. [7] Yim E.-K., Lee K.-Ho, Namkoong S.-E., Um So-J., Park J.-S. *Cancer Letters* (Amsterdam, Netherlands). **2006**, *235(2)*, 209. [8] Fulda S., Friesen C., Los M., Scaffidi C., Mier M., Nuñez, Krammer P.H., Peter M.E., Debatin K.-M. *Cancer Res.* **1997**, *57*, 4956. [9] Hata K., Hori K., Takahashi S. *J. Nat. Prod.* **2002**, *65*, 645. [10] Recio M. K., Giner R.M., Máñez S. et al. *Planta Med.*, **1995**, *61*, 9. [11] Nasonov E.L., Skripnikova I.A., Nasonova V.A. Problem of osteoporosis in rheumatology. Moscow, Stin, **1997**. 429 p.[12] A.G.Shavva, S.N. Morozkina et al. *Russ. J. Bioorg. Chem.* **2007**, *33*, 310.