

DEPARTMENT OF PRECLINICAL AND CLINICAL
PHARMACOLOGY AND TOXICOLOGY
MEDICAL FACULTY, SKOPJE
REPUBLIC OF MACEDONIA

EXPERT'S REPORT FOR TRADITIONAL HERBAL MEDICINE

VARUMIN[®] - 2

The request of preparing the ADDITION TO THE EXPERT'S REPORT for traditional herbal medicine VARUMIN[®] - 2 was submitted by **Inter-evrogeneks, Novo Selo, Republic Macedonia.**

On the base of decision of the Expert collegiums of the Department of Preclinical and clinical Pharmacology and toxicology at Medical Faculty in Skopje, I was chosen to make an EXPERT'S REPORT for traditional herbal medicine VARUMIN[®] - 2, submitted by **Inter-evrogeneks, Novo Selo, Republic Macedonia.**

After the study of the submitted documentation to me and other relevant information I suggest to the Expert collegiums of the department to accept this text like EXPERT'S REPORT for traditional herbal remedy VARUMIN[®] - 2.

1.0 FORM AND COMPOSITION

Form: solution for oral administration

2.0 GENERAL INFORMATION FOR THE PRODUCT

Varumin[®]2 is traditional herbal medicine (solution for oral administration), which in his composition contains water extract from herbal drugs and aloe dry extract, which are in fact their main active components of the herbal remedy.

Varumin[®]2 in combination with Varumin[®]1 is assigned for improving the general state of the organism when exhausted, for increasing the power of resistance, like adjuvant therapy to the standard therapy in various acute and chronic illnesses, malignant diseases, anemias and in other positions which are characterized with lessen immunity and bad general condition.

7.0. EFFECTS OF THE PRODUCT USE

Varumin 2 is traditional herbal remedy for improving of the general state of the body if exhausted, for increasing of the resistance, like adjuvant in standard therapy of acute and chronicle diseases, malignant diseases, anemia and other states that are characterized with lessen immunity and bad general state.

8.0. DOSING AND POSOLOGY

VARUMIN[®] 1 is assigned for oral combine use with product VARUMIN[®]2 as on the scheme:

VARUMIN[®]1: at the beginning of the therapy, drink the whole amount (50 ml) of VARUMIN[®]1. After 6 hours begin to take VARUMIN[®] 2.

VARUMIN[®]2: to take 4 times a day, one soupsoon before meal.

9.0. PRECAUTION OF THE PRODUCT USE

(Joanne Barnes 2002; PDR for Herbal Medicines 2002; WHO 1999).

VARUMIN[®] 1 must not be used at:

- Persons extremely sensitive to some of the components of the preparation;
- Children under than 10 years
- Persons with intestinal obstruction;
- Persons with inflammatory intestinal illnesses (Khron disease, ulcer colit);
- Inflammatory of the appendix (appendicitis) and stomach-ache with enigmatic etiology;
- During pregnancy,

9.2. Interactions

Long term use of aloe preparations together with cardiac glycosides and anti-arrhythmic drugs can take to excessive lose of potassium and to assignee the effect of cardiac glycosides and antiarytmic drugs.

Parallel use of the aloe preparations with tiazide diuretics and corticosteroids increases the possibility of potassium deficient.

Drugs that contain *Viscum album* can stress the effect of the cardiac glycosides, anti hypertensive, anti-depressives and anti-coagulants.

Patients who use at the same time selective inhibitors of the overtaking of the serotonin (exam. sertralin) and preparations based on *St John's worth* the increasing of the level of serotonin is registered. All the knowledge suggested that *St John's* have affection on the hepatic citochrom P450 system, by enlarging of the activity of the isoenzyme CYP3A4, worth may reduce the activity of some medicaments which are used at the same time known as the replacements of that enzyme, lake no sedative antihistamines, oral contraceptives, amprenavire, some antiretroviral medicaments, antiepileptic, Ca-blocators, cyclosporine, some chemotherapeutics, macrolitic, antibiotics and certain antifungal medicaments.

9.3. The measures of precaution and warning

Prolonged use of preparations that contain aloe can provoke:

- hypersensitive reactions which manifest themselves with papular dermatitis and eczematous formations;
- losing of electrolytes (especially potassium), which can result in hyperaldosteronism, inhibition of the intestinal motility and stressing the activity of the cardio active medicaments;
- gastrointestinal difficulties, heart arrhythmia and nephropathies (in rare circumstances);
- albuminuria and chematuria

9.4. Adverse effects

Stomach-ache and spasms can appear in application even if one dose of preparations that contain aloe. Chronicle use of laxatives (like the extract of aloe) can provoke electrolytic misbalance (hypo potassium and hypocalcaemia), metabolite acidosis, and malabsorbtion; lose in weight, albuminurija and chematuria. Weakness and orthostatic hypotension can be expected in aged patients, after long-term of use of extracts of aloe.

Steatorea and gastroenteropathy with hypoalbuminemia are registered at some patients on aloe therapy. Malanotics pigmentation on the colon mucosa (pseudomelanosis coli) is registered at patients who take antrahinon laxatives for long period of time. This pigmentation is from reversible character and is withdrawn after 4-12 months after the interruption of the therapy.

10.0 RATIONALITY OF THE COMBINATION

Varumin® 2 is traditional herbal medicine (solution for oral administration), which in his composition contains water extract from herbal drugs and aloes dry extract, which are the main active components of the herbal remedy. In the sufficient literature there is lots of information which lead to the wide applications of these compounds in traditional and homeopathic, also in scientific medicine.

In the elaborated literature there are no data about the possible interactions or incompatibilities between the composing components of the product.

11.0 PACKAGING

- Glass bottle with 200 ml solution for oral use.

12.0 CONCLUSION

Varumin[®] 2 is preparation (solution for oral administration), which in his composition contains water extract from herbal drugs; aloes dry extract and propolis, which are the main active components of the herbal remedy.

Varumin[®] 2 is traditional herbal medicine which in combination with Varumin[®]1 is assigned for improving of the general state of the body if exhausted, for increasing of the resistance, like adjuvant in standard therapy of acute and chronicle diseases, malignant diseases, anemia and other states that are characterized with lessen immunity and bad general state.

In the sufficient literature for the active compounds of the herbal remedy there are many data which lead to the wide applications of these compounds in traditional and homeopathic, also in scientific medicine. The active ingredients of the product have laxative, anti-inflammatory, anti-microbe, immune-stimulative, detoxificative, citotoxic, diuretic, anti-depressive and other actions. These pharmacodinamic characteristics of the some compounds of the Varumin 2 justified the purposed field of action.

On the base of the above mentioned in this Expert report, I consider that Varumin 2 – product of the company Inter-evrogeneks, Novo Selo, R. Macedonia, fulfilled the conditions on his composition and characteristics, directed for the traditional herbal medicines of that kind and can be registered in R. Macedonia.

The Expert report is made by

Prof. d-r Stojmir Petrov

The Expert collegiums of the Department of Preclinical and clinical Pharmacology and toxicology, on his meeting on the 18.12.2009, make an overview on the text of the EXPERT'S REPORT for traditional herbal medicine VARUMIN[®] - 2, a product of the company Inter-Evrogeneks, Novo Selo, Republic of Macedonia and it has been adopted.

Director
Prof. d-r Petar Milosevski

LITERATURE:

1. Al-Awadi FM et al. On the mechanism of the hypoglycaemic effect of a plant extract. *Diabetologia* 1985; 28:432-434.
2. Al-Awadi FM, Cumaa KA. Studies on the activity of individual plants of an antidiabetic plant mixture. *Acta Diabetol Lat* 1987; 24:37-41.
3. Anon. *Aloe Vera - God's Gift to Mankind!!* 1996.
4. Bloksma N et al. Stimulation of humoral and cellular immunity by *Viscum* preparations. *Planta Med* 1982; 46: 221-227.
5. Blumenthal, M., ed. (1998) *The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines*. Austin, Texas, American Botanical Council, pp. 12, 80-81.
6. Bruneton J. *Pharmacognosy, phytochemistry, medical plants*. Paris lavoisier, 1995.
7. Bruneton J. *Pharmacognosy, phytochemistry, medical plants*. Paris lavoisier, 1995.
8. Bruneton, J. 1995. *Pharmacognosy, Phytochemistry, Medical plants*. Paris: Lavoisier Publishing.
9. Chung J-H et al. Acceleration of the alcohol oxidation rate in rats with aloin, a quinone derivate of aloe. *Biochem Pharmacol* 1996; 52: 1461-1468.
10. Coeugnet EG, Elek E. Immunomodulation with *Viscum album* and *Echinacea purpurea* extracts. *Onkologie* 1987; 10(Suppl.3): 27-33.
11. Davis RH et al. Aloe vera, hydrocortisone and sterol influence on wound tensile strength and anti-inflammation. *Journal of the American Pediatric Medical Association*, 1994, 84:614621.
12. Davis RH et al. Anti-inflammatory and wound healing of growth substance in Aloe vera. *Journal of the American Pediatric Medical Association*, 1994, 84:7781.
13. ESCOP. 1997. "Hyperici herba". *Monographs on the Medicinal Uses of Plant Drugs*. Exeter, U.K.: European Scientific Cooperative on Phytotherapy.
14. *European pharmacopoeia*, 3rd ed. Strasbourg, Council of Europe, 1997.
15. Evans MR, Preece AW. *Viscum album* - A possible treatment for cancer? *Bristol Medico Cbir J* 1973; 88:17-20.
16. Franz H et al. Isolation and properties of three lectins from mistletoe (*Viscum album* L.) *Biochem J* 1981; 195: 481-484.

17. Ghannam N et al. The antidiabetic activity of aloes: preliminary and experimental observations. *Horm Res* 1986; 24: 288-294.
18. Gorunovik M.S. Lukik P. *Farmakognozija*, Beograd 2001.
19. Grindlay D, Reynolds T. The Aloe vera phenomenon: a review of the properties and modern uses of the leaf parenchyma gel. *Journal of ethnopharmacology*, 1986, 16:117-151.
20. Heggors JP, Pelley RP, Robson MC. Beneficial effects of Aloe in wound healing. *Phytotherapy research*, 1993, 7:S48S52.
21. Horgan DJ. Widespread dermatitis after topical treatment of chronic leg ulcers and stasis dermatitis. *Canadian Medical Association Journal*, 1988, 138:336-338.
22. Hormann HP, Korting HC. Evidence for efficacy and safety of topical herbal drugs in dermatology: Part 1: Anti-inflammatory agents. *Phytomedicine*, 1994, 1:161-171.
23. Hulsen H, Mechelke F. In vitro effectiveness of a mistletoe preparation on cytostatic-resistant human leukemia cells. *Naturwissenschaften* 1987; 74:144-145.
24. Hunter D, Frumkin A. Adverse reactions to vitamin E and Aloe vera preparations after dermabrasion and chemical peel. *Cutis*, 1991, 47:193194.
25. Izzo AA et al. The role of nitric oxide in aloe-induced diarrhea in the rat. *Eur J Pharmacol* 1999; 368: 43-48.
26. Joanne Barnes, Linda A Anderson and David Phillipson. *Herbal Medicines, A guide for healthcare professionals; Second Edition*, Pharmaceuticals Press 2002.
27. Khwaja TA et al. Isolation of biologically active alkaloids from Korean mistletoe *Viscum album, coloratum*. *Experientia* 1980; 36:599-600.
28. Khwaja TA et al. Recent studies on the anticancer activities of mistletoe (*Viscum album*) and its alkaloids. *Oncology* 1986; 43(Suppl.1): 42-50.
29. Konopa J et Al. Isolation of viscotoxins. Cytotoxic basic polypeptides from *Viscum album L*. *Hoppe Seyler's Z physiol Chem* 1980; 136:1525-1533.
30. Leung A.Y. and S. Foster. 1996. *Encyclopedia of Common Natural Ingredients Used in Food, Drugs and Cosmetics*, 2nd ed. New York: John Wiley & Sons, Inc.
31. Luther P et al. Isolation and characterization of mistletoe extracts. II. Action of agglutinating and cytotoxic fractions on mouse ascites tumor cells. *Acta Biol Med Ger* 1977; 36:119-125.

32. Luther P et al. Reaktionen emiger annko~rpera.hnllicher Substanzen aus Insekten (Protektine) und Pflanzen (Lektine) mit Aszites-Tumorzellen. *Acta Biol Med Ger* 1973; 31:K11-18.
33. Luther P, Mehnert WH. Zum serologischen Verhalten emiger handelstiblicher Preparate aus *Viscum album L.*, inshesondere des Iscador, in bezug aug menschliche Blutzellen und Aszites Tumorzellen von Mausen. *Acta Biol Med Ger* 1974; 33:351-357.
34. Morrow DM, Rappaport MJ, Strick RA. Hypersensitivity to aloe. *Archives of dermatology*, 1980, 116:10641065.
35. Newall, C.A., L.A. Anderson, J.D. Phillipson. 1996. *Herbal Medicines: A Guide for Health-Care Professionals*. London: The Pharmaceutical Press.
36. Newton LE. In defence of the name *Aloe vera*. *The cactus and succulent journal of Great Britain*, 1979, 41:2930.
37. PDR® For Herbal Medicines. Second Edition, 2002. Medical Economics Company.
38. Petkov V. Plants with hypotensive, antiatheromatous and coronarodilatating action. *Am J Cbjn Med* 1979; 7:197-236.
39. Shelton RM. *Aloe vera*, its chemical and therapeutic properties. *International journal of dermatology*, 1991, 30:679683.
40. Shin KH et aL Elongica-dimers A and B, two potent alcohol metabolism inhibitory constituents of *Aloe arborescens*. *J Nat Prod* 1997; 60:1180-1182.
41. Tucakov J.: *Лечење билљем*. Издавачка Радна Организација, “Рад”, Београд, 1999.
42. Visuthikosol V et al. Effect of *Aloe vera* gel on healing of burn wounds: a clinical and histological study. *Journal of the Medical Association of Thailand*, 1995, 78:403409.
43. WHO Monographs on selected medical plants, Volume 1; 1999.
44. Wichtl, M. and N.G. Bisset (eds.). 1994. *Herbal Drugs and Phytopharmaceuticals*. Stuttgart: Medpharm Scientific Publishers.
45. Yamamoto M et al. Inhibitory effects of aloe extracts on antigen- and compound 48/80-induced histamine release from rat peritoneal mast cells. *Jpn J Toxicol Environ health* 1993; 39:395-400.
46. Ziska P et al. The lecithin from *Viscum album L.* Purification by biospecific affinity chromatography. *Experientia* 1978; 34:123-124.

47. Assessment report on *Aloe barbadensis* and aloe (various species, mainly *Aloe ferox* Mill. and its hybrids), EMEA/HMPC, Doc. Ref. 76313 /2007.
48. Bankova V., Recent trends and important developments in propolis research, *eCAM* 2 (1) 29-32, 2005.
49. Berghofer R., Holzl J., Biflavonoids in *Hypericum perforatum*; Part 1. Isolation of 13,118-biapigenin, *Planta Med.* 53, 216-17, 1987.
50. Berghofer R., Holzl J., Isolation of 13',118-biapigenin (amentoflavone) from *Hypericum perforatum*, *Planta Med.* 55, 91, 1989.
51. Beuers U., Spengler U., Pape G.R., Hepatitis after chronic abuse of senna, *Lancet*, 337-472, 1991.
52. Bombardeli E., Morazzoni P, *Hypericum perforatum*, *Fitoterapija*, 66, 43-68, 1995.
53. Boucard-Maitre Y. et al, Cytotoxic and antitumoral activity of *Calendula officinalis* extracts, *Pharmazie*, 43, 220, 1988 in Newall C., Anderson L., Phillipson D., *Herbal Medicines, A guide for health-care professionals*, The Pharmaceutical Press, London, 1996.
54. British Herbal Pharmacopoeia (BHP), British herbal medicine association, 1996.
55. Bruneton J., *Pharmacognosy, Phytochemistry and Medicinal Plants*, 2nd edition, Intercept Ltd., Londres, Paris, New York, 1999.
56. Capasso F., Gaguinella T., Grandolini G., Izzo A., *Phytotherapy*, Springer, Berlin, Heidelberg, New York, Hong Kong, London, Milan, Paris, Tokyo, 2003.
57. Capasso F. et al., 1983 in Assessment report on *Aloe barbadensis* and aloe (various species, mainly *Aloe ferox* Mill. and its hybrids), EMEA/HMPC, Doc. Ref. 76313 /2007.
58. Casley-Smith J.R., The effect of *Unguentum lymphaticum* on acute experimental lymphoedema and other high-protein edemas, *Lymphology*, 16, 150-6, 1983 in Newall C., Anderson L., Phillipson D., *Herbal Medicines, A guide for health-care professionals*, The Pharmaceutical Press, London, 1996.
59. Chandler R.F. et al., *Ethnobotany and phytochemistry of yarrow, Achillea millefolium*, *Compositae, Economic Bot.*, 36, 203-23, 1982 in Newall C., Anderson L., Phillipson D., *Herbal Medicines, A guide for health-care professionals*, The Pharmaceutical Press, London, 1996.
60. Chen H.C. et al., 2004 in Assessment report on *Aloe barbadensis* and aloe (various species, mainly *Aloe ferox* Mill. and its hybrids), EMEA/HMPC, Doc. Ref. 76313 /2007.

61. De Witte P., Metabolism and pharmacokinetics of antranoids, *Pharmacology*, 47, 86-97, 1993.
62. Dervendzi V., Nasi lekoviti rastenija i nivna upotreba, *Prosvetno delo*, Skopje, 1977.
63. Dewick Paul, *Medicinal Natural Product*, John Wiley and Sons, Chichester, New York, Weinheim, Brisbane, Singapore, Toronto, 1997.
64. Dimov V., Ivanovska N., Manolova N., Bankova V., Nikolov N., Popov S., Immunomodulatory action of propolis. Influence on anti-infectious protection and macrophage function, *Apologie*, 22, 155-62, 1991.
65. Dimov V., Ivanovska N., Bankova V., Popov S., immunomodulatory action of propolis: IV. Prophylactic activity against Gram-negative infections and adjuvant effect of the water-soluble derivative, *Vaccine*, 19, 817-23, 1992.
66. Evans W.C., *Trease and Evans Pharmacognosy*, W. B. Saunders, edonburg, London, New York, Philadelphia. St Luis, Sydney, Toronto, 2002.
67. Godding E.W., Therapeutics of laxative agents with special reference to the antraquinones, *Pharmacology* 14, 78-101, 1976.
68. Gorunovic M., Lukic P., *Farmajkognozija*, Univerzitet u Beogradu, Farmaceutski fakultet, Beograd, 2001.
69. Grange J. M., Davey R. W., Antibacterial properties of propels (bee glue), *J. R. Soc. Med.*, 83, 259-60, 1990.
70. Grimaudo S. et al., 1997 in Assessment report on Aloe barbadensis and aloe (various species, mainly Aloe ferox Mill. and its hybrids), EMEA/HMPC, Doc. Ref. 76313 /2007.
71. Heinrich M., Barnes J., Gibbons S., Williamson E., *Fundamentals of Pharmacognosy and Phytotherapy*, Churcill Livingstone, Edinburg, London, New York, Oxford, Philadelphia, St Luis, Sydney, Toronto, 2004.
72. Hoening J. et al., 1992 in Assessment report on Aloe barbadensis and aloe (various species, mainly Aloe ferox Mill. And its hybrids), EMEA/HMPC, Doc. Ref. 76313/2007.
73. Huber R., Eisenbraun J., Miletzki B., Adler M., Gleiter C.H., Pharmacokinetics of mistletoe lectins – a phase I study, *int. J. Phytoth. Phytopharm.*, 2007 (<http://findarticles.com>).
74. Hulsen H., Mechelke F., In vitro effectiveness of a mistletoe preparation on cytostatic-drug-resistant human leukemia cells, *Naturwissenschaften*, 74, 144-145, 1987.

75. Ishii O., Tanizawa H., Tqakino Y., Studies of Aloe III: Mechanism of laxative effect., Chemical and pharmacological bulletin, 38, 197-200, 1990.
76. Ivanovska N., Stefanova Z., Valeva V., Neychev H., immunomodulatory action of propolis. VII. A comparative study on cinnamic and caffeic acid lysine derivatives, Biol. Immun., 46, 115-7, 1993.
77. Ivanovska N., Neychev h.m, Stefanova Z., Nankova V., Popov S., Influence of cinnamic acid on lymphocyte proliferation, cytokine release and Klebsiella infection in mice, Apologie, 26, 73-81, 1995.
78. Izzo A.A. et al., 1996 and 1999 in Assessment report on Aloe barbadensis and aloe (various species, mainly Aloe ferox Mill. And its hybrids), EMEA/HMPC, Doc. Ref. 76313/2007.
79. Johne a. et al., Interaction of St John's wort extracts with digoxin, in WHO selected monographs of medicinal plants, WHO, Geneve, 2002.
80. Kilic A., Baysallar M., Besirbellioglu B., salih B., Sorkun K., Tanyuksel M., In vitro antimicrobial activity of propolis against methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococcus faecium, Annals of Microbiology, 55, 113-117, 2005.
81. Klein R., Effects of mistletoe extracts on immunocompetent cells in vitro and in vivo, Int. J. Phytotherapy. Phytopharmac., 2007 (<http://findarticles.com>).
82. Kolesnikova A.G., Bacetericidal and immunocorrective properties of plant extract, Zh. Mikrobiol. Epidemiol. Immunobiol., 3, 75-8, 1986. In Newall C., Anderson L., Phillipson D., Herbal Medicines, A guide for health-care professionals, The Pharmaceutical Press, London, 1996.
83. Kujumgiev A., Tsvekova I., Serkedjieva Yu., Bankova V., Christov R., Popov S., Antibacterial, antifungal and antiviral activity of propolis of different geographic origin, J. Ethnopharmacolog., 64, 235-240, 1999.
84. Kulevanova S., Farmakognozija, Kultura, Skopje, 2004.
85. Leung A.Y., Encyclopedia of common natural ingredients used in food, drugs and cosmetics, Wiley, New York, Chichester, 1980.
86. Leuschner J., Preclinical toxicological profile of Hypericum extract LI 160., second International Congress of Phytomedicine, Munich, 1996 in WHO selected monographs of medicinal plants, WHO, Geneve, 2002.
87. Linde K. et al., St John's wort for depression – an overview and meta-analysis of randomized clinical trials, British Medical Journal, 313, 253-258, 1996, in WHO selected monographs of medicinal plants, WHO, Geneve, 2002.

88. Lomgo R. 2002 in Assessment report on Aloe barbadensis and aloe (various species, mainly Aloe ferox Mill. and its hybrids), EMEA/HMPC, Doc. Ref. 76313 /2007.
89. Lukic P., Farmakognozija, 4 dopuveno izdawe, Univerzitet u Beogradu, Farmaceutski fakultet, Beograd, 1988.
90. Miller L., Murray W., Herbal Medicinale, A clinician's guide, Pharmaceutical Product Press, New York, London, 1998.
91. Mills S., Bone K., Principles and Practice of Phytotherapy, Churchill livinstone, Edinburg, London, New York, Philadelphia, St Luis, Sydney, Toronto, 2000.
92. Mishenkova E.L. et al., Antiviral properties of St John's wort and preparations produced from it, in Newall C., Anderson L., Phillipson D., Herbal Medicines, A guide for health-care professionals, The Pharmaceutical Press, London, 1996.
93. Moskalenko S. A., Preliminary screening of far-Easteren ethnomedicinal plants for antimicrobial activity, J. Ethnopharmacol., 15, 231-59, 1986.
94. Muller-Lissner S. A., Adverse effects of laxatives: facts and fiction, Phatrmacology, 47, 138-145, 1993.
95. Nebel A. et al., Potential metabolic interaction between St John's wort and theophylline, Annal of Pharmacotherapy, 33, 502, 1999.
96. Newall C., Anderson L., Phillipson D., Herbal Medicines, A guide for health-care professionals, The Pharmaceutical Press, London, 1996.
97. Okpanyi S.N., Weischer M.L., Animal experiments on the psyhotropic action of a Hypericum extract, Arznmittelforschung, 37, 10-13, 1987.
98. Panossian A.G., Immunosuppressive effects of hypericin on stimulated human leucocytes: inhibition of the arachidonic acid release, leukotriene B4 and interleukin-1 α production and activation of nitric oxide formation, Phytomedicine, 3, 19-28, 1996.
99. Paulino N., dantas A.P., Bankova V. et al., Bulgarian propolis induced analgesic and anti-inflamatory effects in mice and inhibits in vitro contraction of airway smooth muscle, J. Pharmacol. Sciences 93, 307-313, 2003.
100. PDR for Herbal Medicines, second edition, Thomson Physicians Desk References, 2000.
101. Petkov V., Plants with hypotensive, antiatheromatous and coronarodilatating action, Am. J. Chin. Med., 7, 197-236, 1979.
102. Petkov V., Sovremena fitoterapija, Medicina i fizkultura, Sofia, 1982.

103. Piscitelli S.C. et al., Indinavir concentrations and St John's wort, *Lancet*, 355, 547-548, 2000.
104. Sakar M.K. et al., Antimicrobial activities of some hypericum species growing in Turkey, *Fitoterapia*, 59, 49-52, 1988.
105. Samuelsson Gunnar, *Drugs of Natural Origin*, Apotekar societeten, Swedish Pharmaceutical Press, Stockholm, 1999.
106. Scheller S., Gadza G., Pietsz G., Gabrys J., Szumlas J., Eckert L., Shani J., The ability of ethanol extract of propolis to stimulate plaque formation in immunized mouse spleen cells, *Pharmacol. Res. Commun.*, 20, 323-8, 1998.
107. Scheller S., Gadza G., Crol W., Czuba Z., Zajus A., Gabrys J., Shani J., The ability of ethanolic extract of propolis (EPP) to protect mice against gamma irradiation, *Z. Naturforsch. Sect. C. Biosc.*, 44, 1040-52, 1989.
108. Schimmer O. et al., An evaluation of 55 commercial plant extracts in the Ames mutagenicity test, *Pharmazie*, 49, 448-451, 1994.
109. Schimmer O. et al., The mutagenic potencies of plant extracts containing quercetin in salmonella typhimurium TA 98 I TA 100, *Mutation Research*, 206, 201-208, 1988, in WHO selected monographs of medicinal plants, WHO, Geneva, 2002.
110. Schipochliev T. et al., Anti-inflammatory action of a group of plant extracts., *Vet. Med. Nauki*, 18, 87-94, 1981 in Newall C., Anderson L., Phillipson D., *Herbal Medicines, A guide for health-care professionals*, The Pharmaceutical Press, London, 1996.
111. Shipochliev T., Fournadjiev G., spectrum of the anti-inflammatory effect of *Arctostaphylos uva ursi* and *Achillea millefolium*, *Probl. Vutr. Med.*, 12, 99-107, 1984 in Newall C., Anderson L., Phillipson D., *Herbal Medicines, A guide for health-care professionals*, The Pharmaceutical Press, London, 1996.
112. Sforcin J.M., Efeito da sazonalidade sobre as propriedades imunomoduladora e antibacteriana da propolis e perfil bioquímico de ratos, *Veterinaria e Zootecnia*, 1996.
113. Siegers C.P., Anthranoid laxatives and colorectal cancer, *Trends in pharmacological sciences*, 13, 229-231, 1992.
114. Strehl E., Volpert R., elstner E.F., Biochemical activities of propolis extract, *Z. Naturforsch. C.*, 49, 39-43, 1994.
115. Shljahov P., *Pcelarstvo, Nasha kniga*. Skopje, 1990.

116. Stampf J.L. et al. The sensitizing capacity of helenin and two of its main constituents the sesquiterpene lactones alantolactone and isoalantolactone: a comparison of epicutaneous and intradermal sensitizing methods in different strains of guinea pig., *Contact Dermatitis*, 1982 in Newall C., Anderson L., Phillipson D., *Herbal Medicines, A guide for health-care professionals*, The Pharmaceutical Press, London, 1996.
117. Summary report on *Hypericum perforatum*, EMEA/MRL/690/99, 1999.
118. Tavares I.A. et al., 1996 in Assessment report on *Aloe barbadensis* and aloe (various species, mainly *Aloe ferox* Mill. and its hybrids), EMEA/HMPC, Doc. Ref. 76313 / 2007.
119. Tatefuji T., Izumi N., Ohta T., Arai S., Ikeda M., Kurimoto M., Isolation and identification of compounds from Brazilian propolis which enhance macrophage spreading and mobility, *Biol. Pharm. Bull.*, 19, 966-70, 1996.
120. Tucakov J., *Lecenje biljem*, IRO RAD Beograd, 1984.
121. Tyler V.E., *The honest herbal*, 3rd edition, Philadelphia, Strickley, 1993.
122. Wagner H et al., immunostimulating polysaccharides (heteroglycans) of higher plants, *Arzaeimittelforsch*, 35, 1069, 1985 in Newall C., Anderson L., Phillipson D., *Herbal Medicines, A guide for health-care professionals*, The Pharmaceutical Press, London, 1996.
123. WHO monographs on selected medicinal plants, Volume 1, WHO, Geneve, 1999.
124. WHO monographs on selected medicinal plants, Volume 2, WHO, Geneve, 2002.
125. Wichtl M., *herbal drugs and Phytopharmaceuticals*, Medpharm, scientific Publisher, Stuttgart 1994.
126. Zhang L., Tizard I.R., Activation of a mouse macrophage cell line by acemannan: the major carbohydrate fraction from *Aloe vera* gel, *Immunopharmacology*, 35, 119-28, 1996.