CIMICIFUGA RACEMOSA (L.) NUTT. (FAM.: RANUNCULACEAE) (CIMICIFUGA, BLACK COHOSH)

by Lamberto Monti

Cimicifuga Racemosa

BOTANY:	A herbaceous plant indigenous to the eastern regions of North America, over 1 metre in height but it can sometimes exceed 2 metres. The leaves, up to 7 cm in length, are compound and pinnate, with dentate folioles along the edge and subcordate to subcuneate at the base. The small white flowers with numerous stamens are clustered in a long inflorescence in the form of tufts. The subterranean part is made up of a system of thick and knotty rhizomes.
DRUG:	It consists of the rhizome and the dried root of *Cimicifuga racemosa* (L.) Nutt.. The drug is not described in the Italian Pharmacopoeia 11th Ed. or in the European Pharmacopoeia 5th Edition.
CHEMICAL COMPOSITION:	The drug contains characteristic triterpenes based on cycloartenol, such as acteol, acteine, cimigenol, cimicifugoside and (E)-isoferulic acid; the isoflavone formononetin is also present but is not found in the alcoholic extracts of the drug.
PHARMACOLOGY:	The numerous pharmacological studies, conducted mainly with the isopropanolic extract of the drug, have shown an increase in vitro of the proliferation of the cells of human mammary carcinoma at concentrations below 2.5 mg/mL and an inhibition of the proliferation at concentrations greater than 2.5 mg/mL. The same results have been obtained with human mammary carcinoma cells positive for the receptor of oestrogens (MCF-7). When, according to the hypothesis that these results were indicative of oestrogenic activity, the isopropanolic extract of the drug was given to ovariectomized rats, an increase in the weight of the uterus and an increase in the sieric levels of ceruloplasmin was observed. However, the oestrogenic activity was not found in other in vivo experiments. For example, the isopropanolic extract of the rhizome has shown in a recent study that it has no effect on the uterus of rats treated for 17 days. Controversial results were also obtained with formononetin which, in in vitro experiments, showed some affinities for the oestrogen receptor but no oestrogenic activity in vivo. A dichloromethanic extract of a hydroalcoholic extract of the drug, when compared with estradiol for the effects on the oestrogen-dependent functions of the uterus and the brain, reduced the sieric levels of the luteinizing hormone but did not increase the weight of the uterus in the treated animals; the same fraction caused in vitro the sub-regulation of the gene of the a receptor of the oestrogens in the MCF-7 cells. Whether cimicifuga has or not an oestrogenic activity remains, at the present state of research, a question that has not been completely clarified. Studies conducted in rats have suggested that preparations of cimicifuga may induce positive effects on bone structure; recent in vitro tests with the isopropanolic extract have shown that these effects are caused by the stimulation of the production of osteoprotegerin in human osteoblasts.
TOXYCOLOGY:	Literature does not have any data from toxicological studies for individual medication or for repeated medication. An extract of the drug with 40% isopropylic alcohol was not mutagenous in the Salmonella test; teratogenesis has not been observed when there is immunoglobulin administration of the raw drug at the dose of 2 g/kg to gravid rats from the 7th to the 17th day of gestation.
CLINICAL STUDIES:	Many clinical studies have been carried out with different types of extracts of the rhizome of cicmicifuga, generally with the aim of evaluating its efficacy in reducing menopause symptoms. Part of these studies have shown the capacity of the studied extracts to reduce this symptomatology. In a controlled study comparing hormone replacement therapy (conjugated oestrogens) and diazepam, an ethanolic extract of the drug reduced the signs of menopause (heat flushes, nocturnal perspiration, nervousness, headaches and palpitations), the score of the Hamilton scale for anxiety and the score of a scale of self-evaluation of the psychological condition with practically the same efficacy as the standards of reference; the extract and the conjugated oestrogens also reduced the atrophy of the vaginal mucous. In another controlled study vs. placebo, an improvement in the menopause symptoms was observed in 31 women out of 92 treated; the women with serious symptoms did not report any improvements. In a further dose-finding controlled study of an ethanolic extract, 90% of the patients responded to the treatment when assessed according to the Kupperman index; no differences of efficacy between the two doses tested (40 and 127 mg/die) were observed. Forty mg/die of isopropanolic extract administered for 3 months to 64 women in menopause has recently proven to be a valid alternative to hormone replacement therapy (low doses of estradiol administered transdermally) to control the vasomotory symptoms associated with the menopause. In another and just as recent controlled clinical study (n=304), but this time vs. placebo, the isopropanolic extract of cimicifuga proved to be effective in the reduction of menopause symptoms, especially if administered in the first phases of the menopause.
THERAPEUTIC INDICATIONS*:	Symptoms of the menopause such as heat flushes, profuse sweating, sleeping disorders and nervous irritability.
SIDE EFFECTS, CONTRAINDICATIONS, INTERACTIONS, SPECIAL PRECAUTIONS*,:**	Slight gastrointestinal disorders and headaches have been reported after the use of preparations of cimicifuga. A case of myotoxicity has recently been reported associated with the use of a food supplement containing cimicifuga***. Cimicifuga may boost the effect of anti-hypertensive drugs causing hypotension; information on interactions of cimicifuga with other drugs or with laboratory tests are not available. Treatment for more than 6 months is not recommended, unless otherwise medically prescribed. Considering the indications, added to the potential oestrogenic effect with the risk of spontaneous abortion, the use of cimicifuga during pregnancy is not justified; nor is paediatric use justified.
DOSAGGI*,:**	Daily quantities of the extract with isopropanol or with ethanol at 40-60% corresponding to 40 mg of the drug, unless otherwise medically prescribed.

** WHO monographs, 2nd volume.*

*** PDR for Herbal Medicines, 2nd Ed., 2000.*

**** Data from literature.*