PROMOTING SUSTAINABLE USE OF MEDICINAL AND AROMATIC PLANTS FOR LIVELIHOOD IMPROVEMENT AND BIODIVERSITY CONSERVATION THROUGH CAPACITY BUILDING TRAINING PROGRAM, SWAT DISTRICT, KHYBER PAKHTUNKHWA, PAKISTAN

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Rural communities in Swat District, particularly those living in the mountain regions, use MAPs locally for medicinal purposes and for domestic food consumption. In addition, MAPs are traded in the urban markets to generate income. This paper reports on a project aimed at capacity building through awareness raising, trainings, exposure, and developing market linkages to promote the sustainable use of MAPs. The methodology of the survey focused on a series of consultation and coordination meetings with Forest Department. Additionally, Focus Group Discussion were held in each village with MAPs traders, collectors, and people of different age groups. This was followed by field surveys guided by community members. The study reported top twenty MAPs species having high market value and used in indigenous system of medicine by all ethnic groups. These species were traded through formal and informal trade network including cross-border smuggling between Pakistan and Afghanistan. The project covered a range of interventions for its sustainable use and livelihood improvement such as local awareness campaigns, capacity-building training, and community mobilization for conservation of threatened species, formation of MAPs Producer Associations who are directly linked to big buyers for maximizing their net income. Capacity building of the target population was the main intervention undertaken to achieve the overall objectives of the project. Therefore, community participation at all levels of the project was ensured to enhance their knowledge and skills on sustainable harvesting and marketing of MAPs, which represent the prime 'engines of growth' for the local economy. The project has achieved all planned targets, and although it is too early to measure the impact of these activities, it is expected that the project will serve as a strategic investment for income generation through sustainable harvesting and marketing of MAPs for rural communities in remote northern parts of Swat District.

HERBAL MEDICINES: FROM PHARMACOLOGICAL ACTIVITY TO THE CLINICAL EFFICACY

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Herbal medicine is becoming increasingly used not only to enhance general health and well-being, but also to cure specific health problems. Nowadays, more than 600 herbal medicinal preparations (HMP) are included in the Governmental Register of Medicinal Preparations of Russia and are available as therapeutic agents. Providing of evidence on safety, pharmacological activity and clinical efficacy according to modern regulation requirements is a challenging for HMP. In this lecture a clinical evidence for *in vivo* registered activities of oil herbal extracts will be discussed.

Recently, an oil extract of *Leonurus cardiaca* L. (OEL) was developed. Phytochemical profiling of OEL shows the presence of iridoids, and traces of flavonoids — rutin, quercetin and hyperoside. Because of absence of alkaloids OEL was not toxic after acute and chronic administration in mice and rats. Anxiolytic effects of OEL (0.6 mg/kg) in number of pharmacological studies on animals were considered to be similar of that by diazepam (1 mg/kg). Additionally, anti-squeeze protection of OEL (0.25 mg/kg) was noted in mice. The safety of OEL was confirmed in future clinical trials. No negative effects were observed in patients with arterial hypertension accompanied by anxiety and sleep disorders after 4 weeks treatment (1.2 g/day). Positive effects of OEL on psychoemotional status and arterial blood pressure in 50 patients with stage I hypertension were observed 1 week earlier than in patients with stage II hypertension. According to the Clinical Global Impression scale, a significant improvement in the symptoms of anxiety and depression was observed in 32%, and moderate improvement in 48% of patients, respectively. A group of 30 patients was involved in an other clinical trial. No side effects were reported, patients treated with OEL have

noted absence of torpidity and stunned consciousness syndrome as a benefits of OEL comparing with synthetic sedative drugs. After first week of treatment a positive tendency in psycho-emotional conditions of patients was observed and statistically significant difference in treated groups comparing to control was observed starting with 2 weeks of experiment.

Oil extract of *Achillea millefolium* L. herb, *Salvia officinalis* L. leaves, *Hypericum perforatum* L. herb, and *Ledum palusre* L. shoots (OEF) was developed for the treatment of rhinitis and rhinosinusitis. The extract was safe to mice and rats after intranasal acute and chronic administration. In dose depended manner extract inhibited growth of *H. influenzae, S. aureus, Str. Pyogenes*, and *N. meningitidisand*, and was bactericidal to *S. pneumoniae* in dilution 1:10 *in vitro*. Antiviral effect was registered against *Sendai* virus in HeLa L41 cell line. Significant anti-inflammatory effect of OEF was observed in rats with acute rhinitis. Histological evaluation of nasal tissue evidenced about decrease of hyperplasia of epithelium and goblet cells, hypersecretion of slime, infiltration by lymphocytes, plasmocytes and macrophages in treated group. Reparative effect of OEF was shown in model of planar wound in rats. Efficacy of OEF was confirmed in an open-label, randomized, placebo-controlled study. A group of adult patients with acute (20 subjects) and chronic (20 subjects) rhinitis was treated with OEF (2–3 drops, 3 times/day, 12 days). No side effects were reported by patients of booth groups. Statistically significant symptoms relieve of rhinitis were registered in booth groups after 8 days of treatment. Cytological examination confirmed anti-inflammatory activity of OEF. Similar results were observed in the second clinical trial.

Given the long history of the use of herbal medicine and clinical evidence on its efficacy, it seems inevitable that such studies will lead to new and improved therapeutic agents for the treatment of human diseases.

INHIBITORY METABOLIC INTERACTIONS OF MAGNOLOL WITH CYTOCHROME P450 ENZYMES IN HUMAN AND RAT LIVER MICROSOMES

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Herbal extracts and phytochemicals have often been reported to modulate drug metabolizing enzyme activity, leading to herb–drug interactions [1]. Among the various drug metabolizing enzymes, cytochrome P450 monooxygenase (CYP) is typically involved in clinically significant interactions between prescribed drugs and herbs. Magnolol (MAG) is a major bioactive component of *Magnolia officinalis*, which has been reported to possess anticancer, antibacterial, antioxidative and anti-inflammatory activities [2]. However, little information is available regarding the CYP-mediated metabolism of MAG and the inhibition type of MAG on CYP activity in the liver. The objective of this report is to understand the metabolic interactions of MAG with CYP in human liver microsomes (HLM) and rat liver microsomes (RLM).

To evaluate the CYP-mediated metabolism of MAG, the disappearance of MAG in the absence or presence of specific CYP isoform-selective inhibitors was determined in HLM and RLM. The concentrations of MAG in the microsomal samples were determined by using HPLC with UV detector at 280 nm. The IC_{50} value of MAG for the inhibition of CYP activity was determined by nonlinear regression using GraphPad Prism 5.01 software.

In HLM and RLM, CYP2C and 3A subfamilies were significantly involved in the metabolism of MAG, while CYP1A subfamily was not. The relative contribution of phase I enzymes including CYP to the metabolism of MAG was comparable to that of uridine diphosphate glucuronosyltransferase (UGT) in RLM. Moreover, MAG potently inhibited the metabolic activity of CYP1A and 2C subfamilies, while weakly CYP3A subfamily in HLM and RLM. Based on Dixon plot, the inhibition type of MAG on CYP activity in RLM was determined as follows: uncompetitive inhibitor for CYP1A; competitive inhibitor for CYP2C and 3A.

These results could lead to further studies in clinically significant metabolism-mediated MAG–drug interactions.

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