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New Bioactive Molecules for Drugs and Pesticidal Applications from some Indian Medicinal Plants

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Concurrent with human civilization, plants have been their true companions as source of medicine. These plants have contributed significantly in discovery, design and development of several modern medicines. Recent move of society towards nature for the treatment of various diseases where there is no satisfactory cure in modern medicine has diverted the attention of natural/medicinal chemists and biologists to unravel their chemical characteristics and biological activities together in order to define their therapeutic potential in the light of modern pathobiological understandings. This move has led collectively to rediscover, design and refine the therapeutic application of medicinal plants.

During last ten years, we have studied several medicinal plants guided by in vitro based bioassays to delineate the chemistry of medicinal plants responsible for biological activities. This effort has led to identify several potent multiple active medicinal plants , their active fractions and synergistic molecular compositions. We have identified particularly, several free radical scavengers, xanthine oxidase and α-glucosidase inhibitory principles present in substantial yield in Indian Medicinal Plants. Free radicals have been implicated either as causative or fostering factor in several disease conditions, like atherosclerosis, diabetes, cancer, inflammation, Alzheimer's disease and Parkinsonism etc. Xanthine oxidase is considered as important source of free radicals and is observed increased in atherosclerosis, hypercholesterolemia, ischemia-reperfusion, inflammation, hepatitis, carcinogenesis, and aging etc. Similarly, α-glucosidase inhibitors also possess broad-spectrum therapeutic activities like anticancer, antidiabetic, antiviral and antihypertriglyceridemic etc. Presence of multiple active phytochemicals in rich concentrations in some of the medicinal plants therefore offers exciting opportunity for development of novel therapeutics and also provides scientific justification for their use in traditional medicines.

Recently we have examined several medicinal plants used in traditional medicines for leads in drug and pesticidal applications. About 100 new chemical entities have been isolated and tested for various biological activities. As examples 1. *Dichrostachys cinerea* 2. *Piper chaba* and 3. *Plumbago capensis*: the results of investigations on these three medicinal plants on isolation of new chemical entities as well as analogue based preparation of several new compounds, their biological activities and pesticidal properties will be presented:

1. Dichrostachys cinerea

A new isomer of mesquitol was isolated from *Dichrostachys cinerea* in excellent yield. It has shown free-radical scavenging property and α-glucosuidase inhibitory activities but, it could not display xanthine oxidase inhibitory property. However, it was obsereved that acylation of 3-OH group significantly enhanced the α-glucosidase inhibition and displayed xanthine oxidase inhibitory potential. The structure activity

relationship revealed that the degree of lipophilicity played a major role in improving enzyme inhibitory activities. A positive correlation was observed between enzyme inhibitory potential and acyl chain length (upto C-16) of aliphatic esters. One of the acyl derivatives has shown promising antidiabetic acivity in *in vivo* model.

2. *Piper chaba*

Chromatographic fractionation of methanol extract from roots of *Piper chaba* Hunter resulted in the isolation of several new dimeric alkaloids (chabamides) together with 11 known compounds. Cytotoxic activities of all the dimeric amides along with their monomers were evaluated against some cancer cell lines. Two compounds exhibited potent cytotoxicity against COLO-205 cell lines with IC_{50} value of 3.10 μg/ml and 0.018 μg/ml. Biomimetic synthesis has also been carried out via Diels- Alder reaction using copper(II) salts in aqueous medium.

3. *Plumbago capensis*

A bioassay-guided fractionation and chemical examination of chloroform extract of *Plumbago capensis* roots resulted in isolation and characterization of two new naphtaquinone derivatives along with six known compounds. All the compounds were tested for their mosquito larvicidal activity against fourth star larvae of *Aedes aegypti* and compared with that of rotenone. Among tested compounds, isoshinalononone and plumbagin showed excellent toxicity with IC_{50} values of 1.26 and 5.43 μg/ml respectively.

A series of plumbagin derivatives containing amino acid moiety were synthesized under mild esterification conditions in excellent yields and screened for their antifeedant activities in tobacco caterpillar (*Sodoptera litura*) and castor semilooper (*Achaea janta*) using no-choice laboratory bioassay. The parent compound lacked significant activity but the analogues were effective in reducing feeding by the two insect species. The introduction of an N-acetyl-L-amino acid side chain to the Michael adduct of plumbagin at the third position of the quinine moiety significantly increased antifeedant activity.