

*Review Article***Overview of Pharmacological Research Activities in North Eastern States of India in Last 5 Years**

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This brief overview intends to shed light on the nature of research activities in the field of pharmacology undertaken mainly by the pharmacology departments of various medical, veterinary and pharmacy colleges from the states of Assam, Manipur, Meghalaya, Sikkim and Tripura. Both experimental and clinical pharmacological research have been undertaken but experiments on identification and validation of diverse pharmacological activities of medicinal plants used as folklore medicines in the north east have been at the forefront. Drug use surveys, disease burden estimation, drug safety monitoring and investigator initiated small scale clinical studies have enriched our knowledge. The contributions have an important bearing on the overall spectrum of pharmacology research in the country while being relevant and sensitive to the needs of the local population. Emphasis on strengthening the research infrastructure as well as building up research manpower capacity are needed to enable greater involvement of the local community in pharmacological research.

Keywords: Pharmacology; Research; North East India; Clinical Pharmacology; Experimental Pharmacology; Veterinary Pharmacology

Background

In the last five years, research in the field of pharmacology in various North east states of India has been notable. This brief overview intends to shed light on the nature of such research activities mainly undertaken by the pharmacology departments of various medical, veterinary and pharmacy colleges from the states of Assam, Manipur, Meghalaya, Sikkim and Tripura.

Both experimental and clinical pharmacological research has been undertaken but experiments on identification and validation of diverse pharmacological activities of medicinal plants have been in the forefront. Drug use surveys, disease burden estimation, drug safety monitoring and investigator initiated clinical studies have enriched our knowledge.

Research undertaken in the field of pharmacology in medical, pharmacy and veterinary institutes is primarily undertaken as postgraduate

dissertation work. However, some departments have additionally conducted research projects with extramural funding. Despite various constraints in undertaking research in such settings several institutes have made significant contributions.

Methodology

The pharmacology departments of all medical colleges and some veterinary colleges of the North Eastern states of India were requested by email to provide information about their research activities in the last five years in a prescribed format. Based on the information provided by the respective departments, this overview has been compiled. However, we wish to inform the readers that the review mainly highlights the contribution from pharmacology departments of medical colleges and some veterinary institutes and is not exhaustive. Despite our sincere efforts to collate information from various sources some contributions may have been inadvertently missed out and we regret such exclusions.

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Contributions from Assam

Pharmacological research activity has been concentrated mostly in the medical colleges and to some extent in veterinary institutes. The establishment of National Institute of Pharmaceutical Education & Research (NIPER) at Guwahati in 2008 with Gauhati Medical College (GMC) as the mentoring institute, has provided additional impetus to pharmacological and pharmaceutical work. The older medical colleges at Guwahati, Dibrugarh and Silchar offer MD seats in Pharmacology to medical students while NIPER Guwahati, in addition to MS (Pharm) Pharmacology & Toxicology, is offering a PhD program in pharmacology and toxicology to students from a pharmacy background. Much of the research activity is centered around dissertation/thesis projects of the students.

Experimental Pharmacology

In recent years screening of pharmacological activity has been carried out as collaborative projects. The research groups from the institutes have excelled in the field of neuropharmacology. Exploration of neurobehavioral activity of experimental animals and ameliorative effects of various agents on abnormal neurobehavior were studied. Interesting results have emerged from studies (Jangra *et al.*, 2016 and Sulakhiya *et al.*, 2014, 2015, 2016) undertaken on effects of *Honokiol*, a lignan isolated from trees belonging to the genus *Magnolia*, for ameliorating stress, anxiety, depression and liver injury in animal models. Various organ toxicity ameliorating effects of natural agents such as hesperidin, silibinin and silymarin have been documented by Jangra *et al.* (2015). Other notable research areas include epigenetic modification studies and attenuation of oxidative stress and neuroinflammatory cascade in neurodeficit animal models. Kumar *et al.* (2016) undertook research on baicalein on cardiovascular oxidative stress models (Kumar *et al.*, 2016), while Kolati *et al.* (2015) have demonstrated the effects of BAY 11-7082 in attenuating oxidative stress in diabetic nephropathy models. Antala *et al.* (2012), documented effects of *Garcinia indica* fruit extracts in animal models of Parkinson's disease. Ali *et al.* (2015), evaluated the effects of resveratrol in models of depression. The protective effect of silymarin on doxorubicin induced chronic testicular toxicity in rats

was studied by Vijay *et al.* (2013). Sriram *et al.* (2013) have undertaken preliminary work on poly (ADP-ribose) polymerase-1 as a potential new drug target for neurological disorders.

Pharmacological research activity in Assam Medical College, Dibrugarh, has concentrated on screening of medicinal plants (some of them indigenous to the North East) for pharmacological activity. Some of the notable ones have been antiulcerogenic activity of ethanolic extract of rhizome of *Curcuma caesia* and methanolic fruit extract of *Musa sapientum* var. *paradisiaca*, analgesic and acute anti-inflammatory effect of ethanolic extract of leaves of *Paederia foetida*, antidiabetic and antihyperlipidemic effects of ethanolic extract of leaves of *Punica granatum*, seed and pulp of *Eugenia jambolana*, bark of *Terminalia arjuna* and leaf extract of *Ocimum sanctum*, antihyperlipidemic and antioxidant activities of fruit pulp of *Cassia fistula* and *Ipomoea aquatica* and antibacterial activity of the ethanolic extracts of various plants. Psychopharmacological activity of *Solanum torvum* was evaluated by Paul *et al.* (2017).

The output from Silchar Medical College has been related to screening of pharmacological activity of indigenous medicinal plants. Anticonvulsant activity has been screened in animal models of methanolic extract of *Lawsonia inermis* leaves and aqueous extract of *Datura stramonium* leaves. Ethanolic extract of *Mimosa pudica* leaves has been screened for hepatoprotective and hypolipidemic activity (Purkayatha *et al.*, 2016). Antidiabetic and renoprotective action of the ethanolic extract of *Andrographis paniculata* and gastroprotective and antioxidant effects of fruits of *Piper nigrum* have been explored in rat models at Jorhat Medical College.

Clinical Pharmacology

Investigator initiated large scale drug trials have not been undertaken during this period. However some small scale clinical trials and a large number of observational studies have been conducted in the medical colleges, mostly as component of postgraduate curricular requirements.

Faculty and students from Guwahati Medical College, Guwahati, have conducted fairly detailed studies on adverse drug reactions (ADR) in HIV

infected patients, including cutaneous ADRs. Drug use surveys have been conducted including a recently published study on prescribing pattern of analgesics in orthopedic in-patient department. The output from Silchar Medical College has been related to pharmacovigilance, prescription audits and drug use surveys in clinical settings (e.g. antihypertensives, antibiotics, antipsychotics), and also exploration of impact of ADRs on quality of life. A few small scale academic trials have also been conducted in the past few years, such as comparison of ondansetron versus granisetron in postoperative nausea and vomiting and comparison of olanzapine versus amisulpride in out-patient schizophrenia patients. Choudhury and Chakravarty (2016) profiled the antimicrobial susceptibility pattern of methicillin resistant *Staphylococcus aureus* isolates from patients in Silchar Medical College (Choudhury and Chakravarty, 2016).

Researchers from Jorhat medical college have conducted small scale clinical trials on preoperative antibiotic use in laparoscopic cholecystectomy and other abdominal surgeries.

An interdisciplinary study at Assam Medical College, Dibrugarh, by Dhar *et al.* (2012) profiled the antimicrobial resistance pattern of *Klebsiella* spp.

Veterinary Pharmacology

The College of Veterinary Sciences under Assam Agricultural University, Khanapara Campus, Guwahati, has kept up a steady output in validation of indigenous medicinal plants for pharmacological activity with potential veterinary as well as clinical applications. The faculty of the department have undertaken several research projects with funding from Department of Biotechnology (DBT), Indian Council of Agricultural Research (ICAR), National Medicinal Plant Board (NMBP) and Life Science Research Board (LSRB). The research group has also secured an Indian patent for a polyherbal formulation for wound healing (426/KOL/2007 A).

Anthelmintic, anticancer, wound healing, antioxidant, antistress, anxiolytic activities have been screened along with identification of their mechanistic molecular biology actions (Saikia *et al.*, 2017). In veterinary pharmacology the work undertaken by Barua *et al.* (2012, 2013, 2016, 2017) have been

diverse and include in vivo antimycobacterial activity of some folklore medicinal plants of north east Barua *et al.* (2012, 2013, 2016, 2017). In-depth studies on the antistress activity and molecular mechanism of action of the leaf extract of *Elsholtzia communis* in rat brain has been undertaken by Barua *et al.* (2017). Studies on the role of adrenergic neurotransmitters on spontaneous muscular activity in ruminant trematode has been conducted by Saikia *et al.* (2014).

The exploration of anticancer activity of several indigenous plant products from north east has been in focus and research groups have explored the adjuvant potential of agents like curcumin (Kumar *et al.*, 2017), chrysin (Kasala *et al.*, 2016) and nimbolide (Bodduluru *et al.*, 2014) in various experimental cancer models. The effects of naringenin in cancer models by modulating CYP1A1, NF- κ B and PCNA expression have been demonstrated by Bodduluru *et al.* (2016).

The role of curcumin in preventing adverse effects of cancer chemotherapy was undertaken by Kumar *et al.* (2017). The research group demonstrated the beneficial role of curcumin in the prevention of cisplatin induced nephrotoxicity in 7, 12-dimethyl benz[a]anthracene (DMBA) induced breast cancer model in rats.

Contributions From Manipur

The Regional Institute of Medical Sciences (RIMS), Imphal, is a premier medical institute in Manipur and has spearheaded research mainly in experimental pharmacology. The department has undertaken projects with extra mural funding from ICMR, DBT and DST (Government of India).

Experimental pharmacology research undertaken by the faculty and postgraduate students as part of their dissertation work include evaluation of various plant derived products for hepatoprotective, antidiabetic, wound healing, anticonvulsant, antiulcer and antibacterial properties in various experimental animal models (Singh *et al.*, 2015).

In the clinical pharmacology field, Monica S *et al.* (2014) have undertaken work on antibiogram patterns of *Salmonella typhi* from enteric fever patients. Such studies from the region are instrumental in designing future antibiotic stewardship program.

Research on drug assays and therapeutic drug monitoring have been initiated. The contributions in the field of drug safety monitoring in cancer patients from the regional cancer center by Gunaseelan *et al.* (2016) has been of great utility as ethnicity is often considered as an important risk factor towards ADR susceptibility (Gunaseelan *et al.*, 2016; Sharma *et al.*, 2015).

Contribution from Meghalaya

At the North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences (NEIGRIHMS), Shillong, several interdepartmental research projects, both in the field of clinical and experimental pharmacology, have been undertaken.

Pharmacoepidemiological studies of public health importance included a rabies vaccine utilization study in Meghalaya and some focused drug safety monitoring studies in elderly and in dermatology (Brahma *et al.*, 2013; Wahlang *et al.*, 2017). Research in the field of medical education is not much in focus but one group from NEIGRIHMS has undertaken some pilot research activities for assessment of tools for dose calculation and prescribing skills for undergraduate medical students (Das and Sarkar, 2015).

Several collaborative studies for screening of plant products for analgesic, anti-inflammatory, anticonvulsant (Lahon *et al.*, 2015), antidiabetic and cardiovascular activities were also undertaken by the department.

Contribution From Sikkim

Research activities at the Sikkim Manipal Institute of Medical Sciences, Gangtok, are focused on both clinical and experimental pharmacology with institutional and ICMR funding.

The clinical pharmacology contributions from the institute encompass the broad research disciplines of pharmacovigilance and pharmacoepidemiology. Pandey *et al.* (2015) undertook a clinical study to characterize the sociodemographic profile of substance abusers in Sikkim. A drug utilization and treatment adherence study in diabetics was done by Satpathy *et al.* (2016). A study of public health relevance was conducted to characterize the profile of infectious disease markers in blood donors at the

Central Referral Hospital of Gangtok (Adhikari *et al.*, 2010). Sharma *et al.* (2015) have undertaken pharmacovigilance and hemovigilance studies which shall serve as an important drug safety data source from Sikkim (Sharma *et al.*, 2015).

In experimental pharmacology, collaborative research focused on screening and validation of pharmacological activity of various indigenous plant products for anti-inflammatory and anti-ulcer activities in animal models by (Tewari *et al.*, 2014). Additional work in this field is ongoing.

Contribution From Tripura

The Agartala Government Medical College (AGMC) and Tripura Medical College & Dr. B. R. Ambedkar Memorial Teaching Hospital, at Agartala, have initiated some research activities in the last five years.

At AGMC some interdisciplinary pilot projects have been undertaken mainly focused on disease epidemiology and drug use surveys. A clinical study was conducted for evaluating the role of gabapentin as adjuvant analgesic with opioids for neuropathic cancer pain when combined with low-dose amitriptyline in cancer patients.

Das *et al.* (2017) assessed the knowledge, attitude and practice of pharmacovigilance among doctors in their teaching hospital in Tripura. Clinical studies on ADR reporting trends, drug utilization in diabetic patients and generic medicine prescribing habits were undertaken (Das *et al.*, 2017). A collaborative study on the sensitivity pattern of antimicrobials was also done. Comparative clinical studies have been undertaken with metformin versus vildagliptin.

Experimental pharmacology research activities have centered on evaluation of *in-vitro* antioxidant and anthelmintic, antidiabetic, hepatoprotective, laxative activities of indigenous medicinal plant products (Deb *et al.*, 2013).

Conclusion

Review of the pharmacology related research undertaken at medical and veterinary institutes of the north east states of India suggests considerable expansion of such activity in recent years. The main focus remains on screening and validation of various

medical plant products for pharmacological activities. Contributions from the College of Veterinary Sciences, Khanapara, and NIPER Guwahati have been vetted by the scientific community as their work has led to several publications in reputed peer reviewed national and international journals. In the field of clinical pharmacology, drug use surveys were commonly undertaken. Investigator initiated large clinical trials are yet to be undertaken. Further impetus to research can be provided by manpower training in both basic and applied research, strengthening of research infrastructure and encouraging students to take up collaborative research projects with other institutes in the country, while being sensitive to the needs of the local community.

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