COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH (CSIR): INITIATIVES IN NEUROSCIENCES

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Introduction

Neuroscience- the science of nervous system overarches vast spectra of scientific studies of nervous system extending from physical, physiological, genetic, ontogenetic, phylogenic, electrochemical, biochemical to pathological etc. Scientists across the globe are interested in study of every bit of individual neuron, interaction of billions of neurons to computational modeling of neuron functions and individual behavior. In simple words neuroscience can be termed as the scientific study of building blocks of nervous system functions at cellular and organism level.

Through many of its laboratories notably Central Drug Research Institute (CDRI), Centre for Cellular & Molecular Biology (CCMB), Indian Institute of Chemical Biology (IICB), Institute of Genomics and Integrative Biology (IGIB),Indian Institute of Toxicology Research (IITR) ,CSIR has been carrying out neuroscience related research programmes for several years now. Well documented records of the research carried out in this area are available in each of these laboratories's annual report. CSIR laboratories have to their credit several leads and could be called India's leading R&D organizations in this domain. The present article limits itself to the development of present times.

During the immediate past, CSIR has adopted the networked way of functioning to synergistically augment expertise and facilities available in different institutes, beginning from tenth Five year Plan period onwards. Although some labs namely Central Drug Research Institute (CDRI), Centre for Cellular & Molecular Biology (CCMB), Indian Institute of Chemical Biology (IICB), Institute of Genomics and Integrative Biology (IGIB),Indian Institute of Toxicology Research (IITR) have structured research programmes on fundamental and applied aspects of neuroscience, a number of other institutes of CSIR also contribute indirectly to this area. For example, in network programme for "discovery and development of bio-actives from herbals and traditional preparations", the bio-evaluation studies on drugs for nervous system are being undertaken by CDRI and IITR whereas the raw material, i.e. herbal extract or traditional preparation, is being procured and prepared by other laboratories which are not necessarily working in the area of biology. CSIR has established State of Art facilities for conducting basic and applied research related to neuroscience, at its various institutes like CDRI, IICB, IGIB, IITR etc. The major priority areas of research include genetic basis of various neurological disorders, drug discovery and neurotoxicity studies. Furthermore, study protocols for CNS components under Essential Safety Pharmacological Studies have been established at CDRI.

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In addition, CSIR institutes are providing R&D support to other national institutions. It is participating in Golden Triangle Partnership Programme along with Deptt. of AYUSH and ICMR. Under this programme, CSIR owns the responsibility for standardization of selected herbal and herbo-mineral formulations for various disease conditions of nervous system like sleep disorders, slow learning, anxiety neurosis etc, so that the traditional medicines are made globally acceptable in terms of safety, quality and action.

CSIR is contributing substantial funds to the area of neuroscience by funding the laboratory programmes for R&D and imparting training to young researches within CSIR as well as other educational institutions through various extra mural fellowship schemes.

A brief of significant work done at various institutes of CSIR is mentioned below:

Basic R&D related to Neurological disorders

IGIB has been undertaking R&D for deciphering the genetic basis of neurological diseases like ataxia, schizophrenia, bipolar disorders, Huntington's disease etc. A significant variability has been observed among patients in response to antipsychotics, and this variability is caused by a variety of factors. Adopting a pharmacogenomics approach represents a unique opportunity for the prediction of response of patients to antipsychotic drugs by investigating genes implicated with specific symptoms and side effects (Krishna et al., 2007). A network model of the interaction/crosstalk between the neurotransmitter signaling systems has been worked out to study the importance of the genes associated with the molecular mechanisms of the disease and drug response (Gupta et al., 2007). Studies on identification of new genes, new drug targets and mutation analysis for complex genetic diseases likes, Epilepsy, Schizophrenia, and Pharmcogenomics in various neurological diseases is in progress.

The G-protein coupled seroronin$_{1A}$ receptor subtype has been extensively studied at CCMB (Annual report CCMB 2006-07). This has become important target in development of therapeutic agents to treat neuropsychatric disorders such as anxiety & depression. CCMB scientists along with foreign collaborators have monitored the ligand binding of the human serotonin1A receptor stably expressed in CHO cells following treatment with sphingomyelinase enzyme (Jafurulla et al., 2008). These results represent the first report on the effect of sphingomyelinase treatment on the ligand binding activity of this important neurotransmitter receptor. Recently, scientists have monitored the organization and dynamics of hippocampal membranes and their modulation by cholesterol using pyrene fluorescence. These results are relevant in understanding the complex organization and dynamics of hippocampal membranes and could have implications in neuronal diseases characterized by defective cholesterol metabolism (Saxena et al., 2008).

At CDRI some scientist groups are undertaking basic and applied research related to neurobehavioral disorders such as memory disorder, stress disorder,

depression, schizophrenia, anxiety and cerebroavascular problem – stroke (Annual report CDRI 2007-08). IICB is working on structure and function of developing astrocytes so as to study the mechanism of action of intrinsic regulators in the plasticity of astroglial cells, to understand the basis of narcotic addiction towards anti-addictive drug development (Annual report IICB 2007-08). R&D related to molecular basis of neuronal loss in Parkinson's disease, motor neuronal disorders and Huntington's disease etc is also being pursued at IICB. The approach involves delivery of toxins and drugs to discrete neuroanatomical loci in animals, analyses of behavioral abnormalities, neurotransmitter metabolism, reactive oxygen species and cellular events of apoptosis, membrane potential/currents, mitochondrial functions and mitochondrial gene expression. Potent antioxidant action of 7-NI in its neuroprotective effects against MPTP-induced neurotoxicity has been studied at IICB (Thomas et al., 2008).

Neurotoxicity Studies

The basic and applied neuroscience research extending from animal models to *in vitro* test systems has been carried out at Indian Institute of Toxicology Research (IITR). An integrated approach in an interdisciplinary manner has been used that encompasses exploring various aspects of neurotoxicity at molecular and cellular levels in animals and human subjects. The scientists have significantly contributed in understanding the mechanisms of neurotoxic metals and pesticides besides other chemicals. Survey studies on health effects of environmental chemicals including clinical studies have also been performed (Annual report IITR 2006-07).

Drug discovery for various Neurological disorders

Stress has been implicated in the etiopathogenesis of several diseases and various stress models have been developed in rodents simulating the human conditions at CDRI. Scientists at CDRI have been able to identify potential anti-stress agents from plant sources (Annual report IICB 2007-08). The stress-induced alterations in status of anti-oxidant enzymes in different regions of brain, plasma corticosterone, and changes in monoamines in various regions of the brain and glucocorticoids receptor (GR) expression profile have been studied in various models of stress. In the area of memory disorders, some pioneering studies have been undertaken on acetylcholinesterase (AChE), metabolizing enzyme of acetylcholine, in relation to memory function at CDRI (Das et al., 2007). These studies have provided new information augmenting the existing knowledge of memory regulation and an important lead for development of selective anti-dementia drugs. The scientists of CDRI have demonstrated that gugulipid, a clinically used anti-dyslipidemic drug has a potential anti-dementic activity and obtained US and European Patents. A herbal anti-stroke drug identified by CDRI is at an advanced stage of development in collaboration with an industrial partner. CDRI has also developed seven synthetic drugs, which have been approved for marketing. These include centbutindole (neuroleptic), centpropazine (anti-depressant), centbucridine (local anaesthetic) and chandonium iodide (neuromuscular blocking agent), which was jointly developed with Punjabi University. At IICB antiparkinsonian drug screening is a major activity (Annual report IICB 2007-08).

At IITR, a radio-ligand binding assay has been developed for High Throughput Screening of new molecules for their neuropharmacological potential. This facility is functional and has been extensively used for CSIR drug development programme and by some of the leading pharmaceutical companies such as Ranbaxy Laboratories Ltd. and Glenmark Pharmaceuticals. Anti-psychotic potential of herbal preparations are also screened routinely in amphetamine induced mouse model.

Summing up, the aforesaid institutes of CSIR have been working in the area of neuroscience for the past many years and have made substantial contributions. This article is not an exhaustive account of R&D achievements of CSIR institutes but a brief write up about the recent R&D activities being undertaken in the laboratories.

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