INTRODUCTION
Every function of the body is directly or indirectly controlled by central nervous system. The central nervous system consist of innumerable sub-units: neurons. No other biological system matches the human brain for complexity of organisation. Full understanding of integration and operation of approximately ten billion neurons and a greater number of glial cells, that account for the enormously varied and complicated functions of the CNS, represents the ultimate scientific challenge.

The knowledge about the physiological functions of various areas of the CNS is far from adequate. Most of the higher functions of CNS cannot be explained in physiological terms. Although the action of drugs on central nervous system has occupied the attention of pharmacologists for many years but we still have scant knowledge as to how these drugs act.

It is widely considered that the most centrally acting drugs exert their action at synaptic junction in nervous pathways. These synaptic sites are not only highly vulnerable to be the site at which malfunction, which may lead to mental disorder, tends to occur as opposed to the less vulnerable axon's supporting tissues and all bodies. An applied drug may act pre-synthetically to effect neurotransmitter synthesis, storage release or re-uptake. Alternatively, it may act post-synaptically to affect transmitter destruction or re-uptake. It may have a direct agonist or anta-gonist action on post-synaptic membrane or it
may compete with the activity of neutral transmitter. These affect the normal transmission at synapse and thereby produce alternation of nervous function.

The synaptic transmission in the periphery is mediated by specific neurohumoral substances, primarily acetylcholine and norepinephrine. The various central neurotransmitters are acetylcholine, norepinephrine, dopamine and 5-hydroxytryptamine. Besides, several amino acids, such as glutamic acid, α-amino- butyric acid, are central neurotransmitter.

The diseases of CNS have been a major concern to all and are being subjected to intensive investigations. Drugs, that exert their primary effect on CNS, comprise the most widely employed group of pharmacologically active agents. They exert a broad-spectrum of effects ranging from tranquillization, sleep, anesthesia-analgesia anticonvulsant and relaxation of smooth muscles etc. Various neurological syndromes, as diverse in etiology, epilepsy and parkasonian, can be effectively controlled by drug therapy.

The introduction of potent psychotherapeutic drugs in past few decades have revolutionized the basic concepts and the treatment of mental disorders. Drugs, other than those designated as centrally acting, may exert pronounced effects on the CNS as a part of their pharmacological action. Many drugs, used for the peripheral action, also produces side effects that are referable to CNS. No drug, presently available, can cure the under-
lying causes of mental illness. They only suppress their overt symptoms and lessen tension. In this way they produce an improved mental state in mentally disturbed patients.

The exact biochemical mechanism of action of a drug on central nervous system, either depressant or antidepressant, is difficult to explain, because there is no single cellular effect which is common to a particular class of CNS agents. But it is the overall effect that is responsible for psychomemetic effect. Many of these compounds have more than one type of action on nervous system. A relatively small number of compounds have been investigated to correlate the biochemical effects of CNS drug to their pharmacological action.

The pharmacological investigation shows that antidepressant drugs act by increasing the level of cerebral amines, viz., dopamine, 5-hydroxytryptamine and norepinephrine. These agents could possibly interfere with the active site of respiratory enzyme, viz. MAO, acetylcholinesterase and gamma-aminobutyric acid (GABA-T). The demonstration of rise in brain monoamines level follows the possible relationship between biochemical and clinical effect of MAO inhibitor. Various other clinically used antidepressants have been found to block norepinephrine, dopamine or 5-hydroxytryptamine uptake. But there may be other possible mechanisms by which they act.

Recent studies have shown that patients, suffering from depression, have abnormally low amount of cyclic-adenosine-
5-monophosphate (C-AMP) and these amounts were found to increase when patients were treated with antidepressants. 

Epilepsy is not a single disease but a collection of disorders of brain function in which the common denominator is the fit (seizure). It is difficult to control fits with one drug alone and many patients receive multiple therapy. Anticonvulsant drugs act by two biochemical actions, namely, the inhibition of carbonic anhydrase enzyme and the elevation of level of 5-hydroxytryptamine. The anticonvulsant activity of carbonic anhydrase inhibitor was found to depend on catecholamine level in brain. 

It was now known that \( \gamma \)-aminobutyric acid appears to be an important inhibitory transmitter and it is found in nerve terminals, in association with glutamic acid decarboxylase, its synthesizing enzyme. So, the drugs, which penetrate into the brain and mimic or potentiate the action of \( \gamma \)-aminobutyric acid, may be useful in treatment of epilepsy or other central disorder.

The monoamine oxidase inhibitors also exhibit anticonvulsant properties and they also increase the level of 5-hydroxytryptamine. The anticonvulsant drugs, such as Phenytoin (diphenyl hydantoin) and troxidone (trimethadione), could increase the level of 5-hydroxytryptamine, without the inhibition of monoamine oxidase. Studies have revealed that altered acetyl choline metabolism also causes human epilepsy.
A hypnotic is a drug which produces sleep and a very large number of hypnotics are available, e.g., barbiturates, nitrazepam, whereas sedatives are drugs which are used to relieve tension and anxiety and make sleep more possible.

Pain is the most common symptom of disease and is a subjective phenomenon with diverse causes. Like any other reflex, pain sensation are carried from the peripheral structures through afferent (sensory nerve fibre) to the brain where the sensation is perceived, evaluated and necessary response elucidated. The relief of pain is always desirable and a large number of analgesics are used for this purpose. The salicylates, other analgesics and anti-inflammatory remedies are usually referred as antipyretic or non-narcotic analgesics to separate from the narcotic analgesics such as morphine, codeine and pethidine etc. The mechanism of action of salicylates is both, central and peripheral, until recently little was known about how the morphine exert its effect on the CNS. It does inhibit the hydrolysis of acetylcholine and in low concentrations it reduces the release of acetylcholine from nerve endings. It also block the action of 5-hydroxytriptamine. With recent discovery of opiate receptor within the brain, the mode of action of morphine has become easier to explain. It now appears that morphine may be mimicking the action of a chemical, normally produced in the brain, an endogenous opiate which may be enkphalin. Further work of Elide et al. evidenced enkphalin as
neurotransmitter.

The discovery of inter-relationship between the toxic properties and chemical constitution of a drug is perhaps the most momentous of all in the modern drug therapy. The ideal drug, which would perform its desired and specific action in the body without producing any other undesirable effect, is probably an unrealizable dream. When a promising new drug has been found a long and laborious work has been done until some compromise is achieved between undiminished curative and diminished toxic action. The new drugs now-a-days are first subjected on the animals but the results indicate that study of animal toxicity is only a rough indicator of toxicity in man. The present position is, therefore, that animal testing will normally reveal gross toxicity precluding use of drug in man. Thus by alternation of chemical structure and synthesis of wide variety of new compounds will continue the method for the development of new drugs more curative and less toxic than the existing ones.

The most important point in designing new drug, to be observed, is the biological properties of molecule and the structure activity relationship. It is seen that many psychotropic compounds have their curative properties due to the addition of a very simple group. In an attempt to synthesize and develop new drugs, which may have less toxicity and safe for the use of mankind, we have synthesized six series of compounds with diverse chemical structure and evaluated them for their
anticonvulsant activities against pentylene-tetrazole and maximal electroshock induced seizure. These compounds have also been screened, in vitro, against monoamine oxidase (MAO) and succinate dehydrogenase (SDH) inhibitory activities. Attempts have also been made to correlate the structure activity relationship of these compounds with respect to their enzyme inhibitory and pharmacological activities. Following series have been synthesized:

1. 5-[(N-arylcarbamyl)methylmercapto]-4-phenyl-3-(4-pyridyl)-1,2,4-triazoles.
2. 3-(N-arylcarboxamidomethyl)-4-quinazolones.
3. 1-Phenyl-3-(p-carboxyphenyl)-5-methylaminoaryl-thiobarbiturates.
4. 3-Aryl-2-[p-(substituted benzylidene)phenylenediamino]-thiazolid-4-ones.
5. 2-Amino-4-[N-(p-alkoxybenzylidene)sulfanilyl]benzanilide and 4-[N-(o-alkoxybenzylidene)sulfanilyl]-2-[2-methyl-4-oxo-3(4H)-quinazolinyl]-benzanilide.
6. 2-[(1H-indol-3-yl-methylene)hydrazino]-N-arylacetamides.

A considerable number of thiosemicarbazide and thiosemicarbazones have been shown to possess spasmytic, anticonvulsant as well as monoamine oxidase inhibitory activities. The triazoles, cyclized product of thiosemicarbazide, possess CNS, sedative and tranquillizer properties. These observa-
tions led us to the synthesize 5-[(N-arylcarbamyl)methylmercapto]-4-phenyl-3-(4-pyridyl)-1,2,4-triazoles and evaluation of the anti-convulsant activities against pentylene-tetrazole induced seizure and maximal electroshock seizure test. The enzyme inhibitory activity has also been determined in vitro.

It is evident from the literature survey that quinazolone nucleus has an important place in field of non-barbiturate synthetic drugs which are effective against various CNS disorders. It possess higher safety margin than that of phenobarbital. Various other quinazolones have been reported as hypnotic, anti-pyretic and possess the ability to inhibit monoamine oxidase and succinate dehydrogenase activity of rat brain homogenate. These observations prompted us to synthesize 3-(N-aryl-carboxamidomethyl)-4-quinazolones as possible CNS active agent, which were evaluated for their MAO and SDH inhibitory and anticonvulsant activities.

Barbiturates comprise an important and valuable class of CNS depressant drugs frequently used in medical practice. Barbiturates have been found to produce all degree of depression of CNS, ranging from mild sedation to coma. Among these, phenyl-ethylbarbituric acid (phenobarbital) is considered to be the drug of choice for anticonvulsant and sedative effect. Various thiobarbiturates have been reported for the anticonvulsant and SDH inhibitory effects on rat brain homogenate, with the hope that a particular compound is superior regarding its
potency, margin of safety and duration of action, we have synthesized 1-aryl-3-(p-carboxyphenyl)-5-methylaminoaryl-thiobarbitalurate. These compounds have been screened for their pharmacological and biochemical activities.

Thiazoles also possess a wide variety of biological properties. Chloromethiazole has been found clinically useful in the treatment of epilepsy. Various thiazoles have been reported as tranquillizer\(^{27}\) and anticonvulsants.\(^{28}\) Thiazolidinone possesses diverse biological properties, like hypnotic,\(^{29}\) local anesthetic,\(^{30}\) and anticonvulsants.\(^{31}\) Stimulated by these observations, we have synthesized 3-aryl-2-[\(\text{E}-(\text{substituted benzylidene})\)-phenylenediamino]thiazolid-4-ones, with the hope that these compounds might display a high order of CNS properties. These compounds have been evaluated for their anticonvulsant and enzyme inhibitory activities.

Considerable interest has been aroused in quinazolone nucleus by the finding that quinazolone is present in many naturally occurring alkaloids and discovery of methaqualone as a potent hypnotic with the high therapeutic index. Various 4-(3\(H\))-quinazolones have been reported as analgesic,\(^{32}\) and hypotensive.\(^{33}\) Some quinazolones have also been reported as anticonvulsant and to be active against MAO and acetylcholine esterase activities.\(^{34-36}\) Different amides and acetamide derivatives are reported to possess anticonvulsant activities.\(^{37,38}\) Some sulphone derivatives are reported as antibacterial, antifungal and
antimalarial agents. Recently, some 2-alkyl-3-(P-alkoxybenzylideneamino)-diphenylsulphon-quinazolin-4-(3H)-ones have been reported as CNS active compound. 39 These observations encouraged us to synthesize 4-[P-alkoxybenzylidene)sulfanilyl]-2-(2-methyl-4-oxo-3-(4H)-quinazolinyl)-benzanilides and to evaluate these for their monoamine oxidase and succinate dehydrogenase inhibitory and anticonvulsant activities.

Indole derivative possess a wide range of biological properties viz., anticonvulsant, CNS depressant, and analgesic. 40, 41 Some indole hydrazines have been reported as psychotropic agents. Various substituted alkylamines and indole benzylhydrazides have also been reported as effective anticonvulsant.

A careful survey of literature has revealed that some hydrazones, obtained from the hydrazides, possess MAO inhibitory properties. These observations have prompted us to synthesize 2-[(1H-indole-2-yl-methylene)hydrazino]-N-arylacetamide which have further been evaluated for MAO, SDH and anticonvulsant activities.
REFERENCES

2. Proton; Pharma Times 10, No. 9, 17, 1978.


