1. Introduction
1. INTRODUCTION

Substances from natural sources that can modify the behaviour and emotions in human beings have always been topics of intense interest since time immemorial and were initially used in the folklore medicine. Slowly the use of such substances extended to treatment of psychiatric disorders. The early twentieth century saw the birth of numerous synthetic drugs such as chlordiazepoxid, diazepam, lithium, phenothiazines, haloperidol etc for the treatment of various behavioural disorders. Though they show clear efficacy but have the ability to induce a series of undesirable effects like sedation, muscle relaxation, amnesia, interaction with alcohol/barbiturates and dependency- liability. These undesirable effects created the need for better molecules (Stahl, 1998; Richelson, 2001; hardman et al, 2001). Thence, the quest to improve the pharmacotherapy by minimizing side effects and optimizing therapeutic response continued and resulted in late 1990s, the birth of selective serotonin reuptake inhibitors (SSRIs).

Apart from the lack of specific therapy, the other major drawback is the unclear understanding of the neurobiology of these disorders. A better understanding of the causes and pathology of such disorders coupled with rational drug design could provide an excellent tool against combating such diseases.

Anxiety is a state of universal feeling that is part of the everyday human life. Feelings of anxiety and fear are often unpleasant emotions commonly caused by the perception of potential danger that threatens the security of the individual and results in various somatic and autonomic effects like, restlessness and agitation, tachycardia, sweating, weeping, gastrointestinal disorders, sleep disturbances, interference with normal life.

Depression is considered as an affective disorder, characterized primarily by change of mood (depression and mania) rather than thought disturbances.

Epidemiological studies reveal that 25% of individuals develop one or more mental or behavioral disorders at some stage in their life. At present about 4 million adult Americans suffer from Generalized Anxiety Disorder (GAD). Phobia is the most commonly seen anxiety disorder and 49.5% of people reporting an unreasonably strong
fear and 22.7% of those people meeting criteria for simple phobia. Social anxiety disorder (SAD) is the next most common disorder of anxiety, with 13.3% of people reporting symptoms which meet the DSM criteria. It is noteworthy that the prevalence of GAD in India seems to be steepingly high with 8.5% of sufferers in the population.

The prevalence of major depression in the general population is estimated at 5% (Blazer, et al., 1999). At present 121 million people are estimated to suffer from depression. An estimated 5.8% men and 9.5% women experience a depressive episode. Suicide remains one of the most common and unavoidable outcomes of depression with depressive illness being responsible for 60% of death toll (Stahl, 1998; Richelson, 2001; WHO, 2001). More often than not anxiety is generally found to be co-morbid with depression wherein 58% of patients lifetime major depressive illness having at least one anxiety disorder.

These epidemiological data warn the proportion of people who are prone or likely to suffer from various forms of these disorders if care is not taken. Need of the hour is the effective management to curtail the progress of such disorders. However, there are various forms of management available which includes both pharmacological and non-pharmacological.

Current pharmacotherapy of depression and anxiety revolves around use of synthetic molecules as well as drugs from natural sources especially of plant origin. Drugs aimed at treating depression thought to act via three major pathways, viz inhibition of monoamine oxidase enzyme, blockade of reuptake of biogenic amines (5-HT, NE, DA) and blocking post synaptic 5-HT\textsubscript{2A} receptor (Bourin et al., 1996; Stahl, 1998; Richelson, 2001; Hardman, 2001).

However increasing attention is being paid to post synaptic regulation of noradrenergic receptors and the alteration in the GABAergic, serotonergic transmission in the treatment of anxiety and depression. Serotonergic transmission involves a rich diversity of receptor subtypes located either pre- or post-synaptically and are functionally different rather contrasting in many instances (Redrobe and Bourin 1998; Maubach et al., 1999; Blier and ward, 2003).

GABAergic transmission is also explored in great detail because of its biological complexity and molecules that could specifically act at different receptor sites are being
looked at that could mediate definite physiological effects while causing little or no side
effects (Kent et al., 2002; Hardman, 2001). However such a thing remains elusive.

Of late stress has been accepted to be the major cause in the development of these
psychiatric disorders (Holsboer, 1998; McEwen, 2001). However such a thing remains elusive.

Comorbidity of various forms of anxiety and depression with each other and in
some cases, with other psychiatric illness add up to the problems faced by clinicians.
Moreover, various types of anxiety and depression share many clinical and biological
similarities and tend to respond to same treatments (Stahl, 1998; Richelson, 2001;
hardman, 2001).

Despite the advent of new molecules in pharmacotherapy of anxiety and depression,
it is unfortunate that both these disorders go underrated, undiagnosed and untreated.
Currently prescribed molecules though provide some improvement in clinical state of the
patient but come with the burden of adverse events (Stahl, 1998; Hardman, 2001). To add
to this burden, it is difficult to predict which patient will respond to any given treatment. It
is reported that only two out of three patients respond to any given treatment, out of which
one is likely to respond to placebo alone (Stahl, 1998; Walker and Edwards, 1999). On
the other hand drugs obtained from natural origin are perceived to have least risk and side
effect profiles and yet claim to cure psychiatric disorders much the same way as their
synthetic counterparts.

Some of the examples of the drugs employed for this purpose are, St. Joh’s wort,
Ginseng, Ginko biloba, kava, Saw palmetto, Euphorbia hirta, Shilajit, Valerian,
Convulvulus etc. They are used either as monoextracts or as polyherbal preparations
combining two or three plant based medications. Among the polyherbal preparations the
popularly reported ones are Mentat, GS-02, St. John’s wort etc (vandenbogaerde et al.,
2000). The present study aims to explore such a polyherbal formulation, TRAN-01. So far
there were no pharmacological evidences to demonstrate the behavioural effect of this
investigational herbal preparation, Trans-01. However, there are reports, for some of the
ingredients of this formulation, for varied CNS effects.

Hence, the present work was planned to investigate the effectiveness of this herbal
preparation in a variety of animal models depicting psychological anomalies, anxiety and
depression.