INTRODUCTION
1. Depression

A depressive disorder is an illness that involves the body, mood, and thoughts. It affects the way a person eats and sleeps, the way one feels about oneself, and the way one thinks about things. A depressive disorder is not the same as a passing blue mood. It is not a sign of personal weakness or a condition that can be willed or wished away. People with a depressive illness cannot merely "pull themselves together" and get better. Without treatment, symptoms can last for weeks, months, or years. Appropriate treatment, however, can help most people who suffer from depression.(1)

1.1 Types of Depression (2)

Major depression is manifested by a combination of symptoms that interfere with the ability to work, study, sleep, eat, and enjoy once pleasurable activities. Such a disabling episode of depression may occur only once but more commonly occurs several times in a lifetime.

A less severe type of depression, dysthymia, involves long-term, chronic symptoms that do not disable, but keep one from functioning well or from feeling good. Many people with dysthymia also experience major depressive episodes at some time in their lives.

Another type of depression is bipolar disorder, also called manic-depressive illness. Not nearly as prevalent as other forms of depressive disorders, bipolar disorder is characterized by cycling mood changes: severe highs (mania) and lows (depression). Sometimes the mood switches are dramatic and rapid, but most often they are gradual. When in the depressed cycle, an individual can have any or all of the symptoms of a depressive disorder. When in the manic cycle, the individual may be overactive, over talkative, and have a great deal of energy. Mania often
affects thinking, judgment, and social behavior in ways that cause serious problems and embarrassment. For example, the individual in a manic phase may feel elated, full of grand schemes that might range from unwise business decisions to romantic sprees. Mania, left untreated, may worsen to a psychotic state.

1.2 Symptoms of Depression and Mania (3)

Not everyone who is depressed or manic experiences every symptom. Some people experience a few symptoms, some many. Severity of symptoms varies with individuals and also varies over time.

**Depression**

- Persistent sad, anxious, or "empty" mood
- Feelings of hopelessness, pessimism
- Feelings of guilt, worthlessness, helplessness
- Loss of interest or pleasure in hobbies and activities that were once enjoyed, including sex
- Decreased energy, fatigue, being "slowed down"
- Difficulty concentrating, remembering, making decisions
- Insomnia, early-morning awakening, or oversleeping
- Appetite and/or weight loss or overeating and weight gain
- Thoughts of death or suicide; suicide attempts
- Restlessness, irritability
- Persistent physical symptoms that do not respond to treatment, such as headaches, digestive disorders, and chronic pain

**Mania**

- Abnormal or excessive elation
• Unusual irritability
• Decreased need for sleep
• Grandiose notions
• Increased talking
• Racing thoughts
• Increased sexual desire
• Markedly increased energy
• Poor judgment
• Inappropriate social behavior

1.3 Causes of Depression (3)

Some types of depression run in families, suggesting that a biological vulnerability can be inherited. This seems to be the case with bipolar disorder. Studies of families in which members of each generation develop bipolar disorder found that those with the illness have a somewhat different genetic makeup than those who do not get ill. However, the reverse is not true: Not everybody with the genetic makeup that causes vulnerability to bipolar disorder will have the illness. Apparently additional factors, possibly stresses at home, work, or school, are involved in its onset.

In some families, major depression also seems to occur generation after generation. However, it can also occur in people who have no family history of depression. Whether inherited or not, major depressive disorder is often associated with changes in brain structures or brain function.

People who have low self-esteem, who consistently view themselves and the world with pessimism or who are readily overwhelmed by stress, are prone to depression. Whether this represents a psychological predisposition or an early form of the illness is not clear.
In recent years, researchers have shown that physical changes in the body can be accompanied by mental changes as well. Medical illnesses such as stroke, a heart attack, cancer, Parkinson's disease, and hormonal disorders can cause depressive illness, making the sick person apathetic and unwilling to care for his or her physical needs, thus prolonging the recovery period. Also, a serious loss, difficult relationship, financial problem, or any stressful (unwelcome or even desired) change in life patterns can trigger a depressive episode. Very often, a combination of genetic, psychological, and environmental factors is involved in the onset of a depressive disorder. Later episodes of illness typically are precipitated by only mild stresses, or none at all.

1.4 Diagnostic Evaluation and Treatment (4)

The first step to getting appropriate treatment for depression is a physical examination by a physician. Certain medications as well as some medical conditions such as a viral infection can cause the same symptoms as depression, and the physician should rule out these possibilities through examination, interview, and lab tests. If a physical cause for the depression is ruled out, a psychological evaluation should be done, by the physician or by referral to a psychiatrist or psychologist.

A good diagnostic evaluation will include a complete history of symptoms, i.e., when they started, how long they have lasted, how severe they are, whether the patient had them before and, if so, whether the symptoms were treated and what treatment was given. The doctor should ask about alcohol and drug use, and if the patient has thoughts about death or suicide. Further, a history should include questions about whether other family members have had a depressive illness and, if treated, what treatments they may have received and which were effective.
Last, a diagnostic evaluation should include a mental status examination to determine if speech or thought patterns or memory have been affected, as sometimes happens in the case of a depressive or manic-depressive illness.

Treatment choice will depend on the outcome of the evaluation. There are a variety of antidepressant medications and psychotherapies that can be used to treat depressive disorders. Some people with milder forms may do well with psychotherapy alone. People with moderate to severe depression most often benefit from antidepressants. Most do best with combined treatment: medication to gain relatively quick symptom relief and psychotherapy to learn more effective ways to deal with life's problems, including depression. Depending on the patient's diagnosis and severity of symptoms, the therapist may prescribe medication and/or one of the several forms of psychotherapy that have proven effective for depression.

Electroconvulsive therapy (ECT) is useful, particularly for individuals whose depression is severe or life threatening or who cannot take antidepressant medication. ECT often is effective in cases where antidepressant medications do not provide sufficient relief of symptoms. In recent years, ECT has been much improved. A muscle relaxant is given before treatment, which is done under brief anesthesia. Electrodes are placed at precise locations on the head to deliver electrical impulses. The stimulation causes a brief (about 30 seconds) seizure within the brain. The person receiving ECT does not consciously experience the electrical stimulus. For full therapeutic benefit, at least several sessions of ECT, typically given at the rate of three per week, are required.

1.5 Medications

An antidepressant is a psychiatric medication used to alleviate mood disorders, such as major depression and dysthymia. Drugs including the monoamine oxidase
inhibitors (MAOIs), tricyclic antidepressants (TCAs), tetracyclic antidepressants (TeCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) are most commonly associated with the term. These medications are among those most commonly prescribed by psychiatrists and other physicians, and their effectiveness and adverse effects are the subject of many studies and competing claims. Many drugs produce an antidepressant effect, but restrictions on their use have caused controversy and off-label prescription a risk, despite claims of superior efficacy.

Most typical antidepressants have a delayed onset of action (2–6 weeks) and are usually administered for anywhere from months to years. Despite the name, antidepressants are often used to treat other conditions, such as anxiety disorders, obsessive compulsive disorder, eating disorders, chronic pain, and some hormone-mediated disorders such as dysmenorrhea. Alone or together with anticonvulsants (e.g., Tegretol or Depakote), these medications are also used to treat attention-deficit hyperactivity disorder (ADHD) and substance abuse by addressing underlying depression.

Other medications that are not usually called antidepressants, including antipsychotics in low doses (5) and benzodiazepines, (6) may be used to manage depression, although benzodiazepines may cause physical dependence if treatment is not properly monitored by a doctor. Stopping benzodiazepine treatment abruptly can cause unpleasant withdrawal symptoms. An extract of the herb St John's Wort is commonly used as an antidepressant, although it is labeled as a dietary supplement in some countries. The term antidepressant is sometimes applied to any therapy (e.g., psychotherapy, electro-convulsive therapy, acupuncture) or process (e.g., sleep disruption, increased light levels, regular exercise) found to improve a clinically depressed mood.
In the United Kingdom the use of antidepressants increased by 234% in the 10 years up to 2002. (7) In the United States a 2005 independent report stated that 11% of women and 5% of men in the non-institutionalized population (2002) take antidepressants(8) A 1998 survey found that 67% of patients diagnosed with depression were prescribed an antidepressant.(9) A 2007 study suggested that 25% of Americans were overdiagnosed with depression, regardless of any medical intervention.(10) The findings were based on a national survey of 8,098 people.

A 2002 survey found that about 3.5% of all people in France were being prescribed antidepressants, compared to 1.7% in 1992, often for conditions other than depression and often not in line with authorizations or guidelines(11) Between 1996 and 2004 in British Columbia, antidepressant use increased from 3.4% to 7.2% of the population.(12) Data from 1992 to 2001 from the Netherlands indicated an increasing rate of prescriptions of SSRIs, and an increasing duration of treatment.(13) Surveys indicate that antidepressant use, particularly of SSRIs, has increased rapidly in most developed countries, driven by an increased awareness of depression together with the availability and commercial promotion of new antidepressants.(14) Antidepressants are also increasingly used worldwide for non-depressive patients as studies continue to show the potential of immunomodulatory, analgesic and anti-inflammatory properties in antidepressants.

The choice of particular antidepressant is reported to be based, in the absence of research evidence of differences in efficacy, on seeking to avoid certain side effects, and taking into account comorbid (co-occurring) psychiatric disorders, specific clinical symptoms and prior treatment history.(15)

It is also reported that, despite equivocal evidence of a significant difference in efficacy between older and newer antidepressants, clinicians perceive the newer drugs, including SSRIs and SNRIs, to be more effective than the older drugs
(tricyclics and MAOIs).

A survey in the UK found that male general physicians were more likely to prescribe antidepressants than female doctors.

**Most commonly prescribed antidepressants**

The most commonly prescribed antidepressants in the US retail market in 2007 were:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand</th>
<th>Class</th>
<th>2007 Prescriptions (in millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sertraline</td>
<td>Zoloft</td>
<td>SSRI</td>
<td>29.652</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>Lexapro</td>
<td>SSRI</td>
<td>27.023</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Prozac</td>
<td>SSRI</td>
<td>22.266</td>
</tr>
<tr>
<td>Bupropion</td>
<td>Wellbutrin</td>
<td>NDRI</td>
<td>20.184</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Paxil</td>
<td>SSRI</td>
<td>18.141</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Effexor</td>
<td>SNRI</td>
<td>17.200</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Celexa</td>
<td>SSRI</td>
<td>16.246</td>
</tr>
<tr>
<td>Trazodone</td>
<td>Desyrel</td>
<td></td>
<td>15.473</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>Elavil</td>
<td>TCA</td>
<td>13.462</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Cymbalta</td>
<td>SNRI</td>
<td>12.551</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Remeron</td>
<td>TeCA</td>
<td>5.129</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>Pamelor</td>
<td>TCA</td>
<td>3.105</td>
</tr>
<tr>
<td>Imipramine</td>
<td>Tofranil</td>
<td>TCA</td>
<td>1.524</td>
</tr>
</tbody>
</table>

The most commonly prescribed antidepressant in Germany is reported to be (concentrated extracts of) hypericum perforatum (St John's Wort).

In the Netherlands, paroxetine, marketed as Seroxat among generic preparations, is the most prescribed antidepressant, followed by the tricyclic antidepressant amitriptyline, citalopram and venlafaxine.
There are several types of antidepressant medications used to treat depressive disorders. These include newer medications—chiefly the selective serotonin reuptake inhibitors (SSRIs)—the tricyclics, and the monoamine oxidase inhibitors (MAOIs). The SSRIs—and other newer medications that affect neurotransmitters such as dopamine or norepinephrine—generally have fewer side effects than tricyclics. Sometimes the doctor will try a variety of antidepressants before finding the most effective medication or combination of medications. Sometimes the dosage must be increased to be effective. Although some improvements may be seen in the first few weeks, antidepressant medications must be taken regularly for 3 to 4 weeks (in some cases, as many as 8 weeks) before the full therapeutic effect occurs.

Patients often are tempted to stop medication too soon. They may feel better and think they no longer need the medication. Or they may think the medication isn’t helping at all. It is important to keep taking medication until it has a chance to work, though side effects may appear before antidepressant activity does. Once the individual is feeling better, it is important to continue the medication for at least 4 to 9 months to prevent a recurrence of the depression. Some medications must be stopped gradually to give the body time to adjust. Never stop taking an antidepressant without consulting the doctor for instructions on how to safely discontinue the medication. For individuals with bipolar disorder or chronic major depression, medication may have to be maintained indefinitely.

Antidepressant drugs are not habit-forming. However, as is the case with any type of medication prescribed for more than a few days, antidepressants have to be carefully monitored to see if the correct dosage is being given. The doctor will check the dosage and its effectiveness regularly.
1.6 Non Compliance in patients with depression

Around 50% of patients with schizophrenia do not fully comply with treatment and non compliance is linked to relapse, rehospitalisation, poor outcome and high economic cost. The health belief model views non compliance as a decision made by the patients, arrived at after weighing the perceived risk and benefit of the treatment..(21)

Patient compliance may be defined as "The extent to which a persons behaviour coincide with the medical advice he / she has received. Noncompliance with treatment i.e. anything less than full compliance, can take many forms such as failure to attend clinic, refusal to enter hospital, failure to begin a treatment program, premature cessation of treatment and incomplete performance of instruction. With specific reference to medication, non compliance encompasses failure to fill prescription, refusal to take medicine, stopping medication prematurely and taking wrong amount of medication at wrong time.(22)

Atleast half of patients prescribed long term medication for chronic disease do not fully comply with treatment and the proportion is remarkable consistent across disease as disparate as epilepsy, arthritis, dibetis, and asthama. Non compliance is more likely when the treatment goal is to prevent symptom recurrence or Illness relapse. Depression is no exception to this pattern of treatment compliance.

Improving compliance with treatment is a major challenge in the management of schizophrenia and has been recognised as an important issue for more than a quarter of century.(23)

1.6.1 Factors affecting compliance in schizophrenia

Research studies indicate that several factors may influence the likelihood of treatment compliance in patients with chronic psychotic disorders. within the

Taste masking formulation development & stability assessment of antidepressant drug – Paroxetine Hydrochloride
health belief model, these factors can be defined as those concerning patients' belief that they have a psychotic disorder and/or treatment may offer benefits, the perceived cost of treatment, and the availability of reminders or cues to comply with treatment. (24)

**Perceived risk of illness and benefit of treatment**

The belief that treatment may reduce the severity of symptoms or prevent relapse often influences compliance in some patients. Poor compliance have been reported in patients with a lack of insight and awareness of their illness and in those who believe that medicine should be taken only when they were feeling ill, that medication would cause physical harm or that taking medicine is unnatural.

One problem in the treatment of schizophrenia is that relapses often do not occur for several months after the patients stop taking medications. Patients may therefore fail to associate noncompliance with the loss of drugs beneficial effects. (25)

**Perceived Costs of treatment**

Side effects: There is a growing awareness of the potential health risk associated with atypical antipsychotics, especially weight gain, endocrine abnormalities and cardiovascular side effects. It is important to remember that patients would have no reason to know about some of these potential medication risk unless explicitly informed by their healthcare provider or may not recognize a medical complication such as weight gain as side effect.

Antipsychotic side effects are consistently associated with non-compliance or reluctance to accept treatment in patients with schizophrenia. High scores on side effect rating scales have been reported to predict non-compliance in several studies.
and the proportion of patients citing side effects as their primary reason for noncompliance ranges between one quarter and two thirds. (26)

**Negative Subject response**

The subjective response to antidepressant could be defined as the effect of the drug on the patients perception of well being. It is recognized that standard antidepressant can produce a negative subject response. This response is variable but clearly perceived as unpleasant and the patients may fill that the medicine is worsening his conditions. It appears to be a common reaction to acute antipsychotic treatment. This negative subjective response is strongly correlated with poor compliance (27)

**1.6.2 Improving compliance**

Compliance in schizophrenia treatment has received relatively little research attention until recently. However, there is growing evidence that psychosocial interventions, such as education for patients and their families can substantially improve both compliance and outcome. Several environmental factors, however, can address these obstacles to treatment compliance. In particular, the simpler the treatment regimen, the higher the likelihood of compliance eg compliance is enhanced by the use of depot regimens. Social isolation living alone and poor housing are all associated with non-compliance, whereas patients with a support of relative, a spouse or friends are more likely to comply with medications than patients lacking such support. (28)

Paroxetine; (3S, 4R)-3-[(1, 3-benzodioxol-5-vloxy) methyl]-4-(4-fluorophenyl) piperidine is a new generation antidepressant drug. It exerts its antidepressant effect through a selective inhibition for the reuptake of the neurotransmitter serotonin by the presynaptic receptors. Paroxetine is comparable to the tricyclic antidepressants in their clinical efficacy, however, paroxetine is safer and has
greater acceptance by the patients. It is also prescribed in the treatment of related disorders, such as obsessive-compulsive disorder, panic fits, social phobia, and posttraumatic stress. Paroxetine is devoid of sedative effect and remarkably safe in overdose. Paroxetine takes 5.2 hours to reach the peak, with extended half-life (21 hours) that allowed the introduction of formulations for once-daily dosing. These combined qualities made paroxetine the most widely prescribed antidepressants. Literature suggest the highly bitter taste of Paroxetine hydrochloride owing to which it cannot be administered to patients without their knowledge.