Pharmacotherapy is a traditional healing paradigm based mainly on herbs, with numerous pharmacopoeia being compiled over the centuries. It was the dominant therapeutic option until superseded by modern chemical-based conventional drug therapy. As it is now experiencing a revival for reasons, such as better patient tolerance, more information is required on the mode of action and clinical efficacy of herbal remedies. In his Canon of Medicine, Ibn Sina details Tibb pharmacotherapy, allocating specific therapeutic herbs to different categories, or orders, of clinical efficacy and patient safety, based on the temperamental and humoral theories. Western drugs act on specific tissue receptors, whereas herbal remedies exert their action by restoring homeostasis via qualitative and humoral changes. Furthermore, herbal remedies support inner healing, or physis, so differ from Western drugs, which tend to oppose it. They also contain a wide range of active ingredients, which allow for a wide spectrum in pharmacotherapy effect. Consequently, Tibb pharmacotherapy is better tolerated, and less prone to adverse drug reactions.

**INTRODUCTION**

Pharmacotherapy is without a doubt an important therapeutic option for the treatment of the majority of most disorders (Chisholm-Burns, 2016). The use of herbs and other natural products goes back as far as civilisation itself. In the search for food, and to cope successfully with suffering, humans learnt to distinguish between plants which were useful as food, and those with healing properties (Ody, P, 1993). This mutually advantageous relationship between the plant kingdom and humankind has resulted in many plants being used as valuable remedies (Hoffman, D, 2013).

“God in his infinite goodness and bounty hath by the medium of Plants, bestowed almost all food, clothing and medicine upon man” [Gerarde’s Herbal (1636)]

Pharmacotherapy has been around for thousands of years. Virtually every society and culture has adopted it in one form or another. Even today, in spite of the massive inroads achieved by Western medicine and synthetic drug usage, around 80% of the world’s population uses herbal medication to a greater or lesser extent (Chevallier A, 1996). It was only with the arrival of the first industrial revolution in the 18th Century and the advent of Western medicine in the 20th that herbal medicine was progressively relegated to a minor role, especially in the developed world (Chikezie PC et al., 2015).

**History of Tibb Pharmacotherapy:** The History of pharmacotherapy in Tibb began more than ten thousand years ago in the Middle Eastern regions of Assyria, Babylonia and Egypt. Over the centuries other countries also contributed to its development; especially the Indian subcontinent (Bhikha R and Haq A, 2000). The cataloguing of traditional remedies into pharmacopoeias was carried out in various parts of the world, with detailed explanations of how they exerted their beneficial actions on the basis of their intrinsic qualities, their practical usage, and any unwanted effects that could be expected (International Meeting of World Pharmacopoeias, 2012). Ibn Sina, in Volume 2 of the *Canon of Medicine* (Bakhtiar L, 1999), detailed a vast number of herbal and non-herbal remedies available at the time. Much of the information contained in the *Canon* draws on several sources, especially Greek texts of the philosopher-physician Dioscorides (40-90 CE) (Norton S, 2006).
Some of these findings are elaborated in the table: Each of these categories has a wide range of pharmacological actions, and many overlap in terms of their activity. In addition, most herbs contain not only one but usually several active ingredients under the same category. Listed below are examples of a few common herbs which contain some of the above categories, bearing in mind that each category may have several active ingredients.

- **Garlic** contains flavonoids, alkaloids, saponins, tannins and cardiac glycosides (Duke JA, 2002).
- **Ginger** contains phenolic compounds, flavonoids, alkaloids, glycosides, saponins and tannins (Schulick P, 2001).
- **Basil** contains terpenoids, alkaloids, flavonoids, tannins, saponins and ascorbic acid (Wagner W, 2015).

The many categories (together with the different active ingredients within each category), contained in a single herb allows for a wide range of pharmacological activity, across multiple physiological systems of the body – cardiovascular, digestive, respiratory, etc. (Bhikha R and Glynn J, 2018). They not only address the signs and symptoms of the illnesses associated with the different systems, but also restore homeostasis at a cellular/sub-cellular level. In addition to their active constituents, medicinal herbs also contain numerous metabolic precursors in the form of primary constituents, such as carbohydrates, fats and proteins, as well as secondary metabolites (Craig WJ, 1999). The therapeutic benefits these collectively confer are unbelievably complex and pose formidable challenges to pharmacological research. Even with the technological advancements of today there is a limited understanding of how the body’s genetically programmed inbuilt wisdom that is, physis, operates (Chishti GM, 1991). The wide range of active substances present in herbal remedies, whether administered singly or in combination, acts positively on several clinical disorders, which on first appearance appear unrelated etiologically (Ody, P, 1993; Chishti GM, 1991). Individually, any one of the active ingredients from the different categories most likely has a narrow spectrum of clinical activity, however, collectively the combined active ingredients from the various categories, act holistically on several disorders at a cellular/sub-cellular, humoral level (Glynn J and Bhikha R, 2017). Garlic, for example, has proven benefits in patients suffering from multiple clinical disorders (Duke JA, 2002); Surendran S,
In the past it was extolled as an invigorating heart tonic, as a reliable laxative, and as a topical anti-microbial agent. More recently, its ability to reduce raised blood pressure, prevent stroke, lower cholesterol, control inflammation, counteract skin and intestinal infections and reduce tumour progress has been confirmed. The basis for these claims lies in the active ingredient’s found in the different categories from Table 1.

The development of Western pharmacology: The development of Western pharmacology has been comprehensively described (Gaitonde BB et al., 2012; Goodman and Gilman’s Manual, 2014). As a genuine scientific discipline, Western pharmacology is little more than 150 years old. It is a broad science of the biological properties of natural substances, synthetic chemicals and drugs, and their effects on the body’s structure, function, and metabolism. It emerged as an independent science in its own right following advances in chemistry, physiology and biology in the late 19th and early 20th centuries, mainly in the West. The development of modern pharmacology began with the solvent extraction of pure substances from medicinal plants at the beginning of the 19th century. The real breakthrough came with the arrival of the synthetic dye industry when some of the dyes were found to have properties of binding to living tissue. This ultimately led to the development of many early drugs. Paul Erlich (1854-1915) was the key figure on the development of modern pharmacology. He described the search for the “magic bullet”, a selective synthetic chemical which would cure syphilis while leaving the sufferer unscathed. He postulated the existence of chemo-receptors, structures located in living tissue which are different in humans than in microbes, parasites and cancer cells. These differences, he thought, could be exploited therapeutically. This heralded the birth of chemotherapy and foreshadowed the receptor theory of drugs.

Western pharmacology emerged from two distinct lines of scientific endeavour: (a) identification, extraction and modification of active ingredients found in plants; and (b) the application of powerful techniques in synthetic organic chemistry. The drugs developed from the identification, extraction and modification of active ingredients from plant origin include morphine, quinine, aspirin atropine and reserpine. Advances in synthetic organic chemistry resulted in the synthesis of a steady stream of “new-to-nature” chemical entities. Barbiturates, for instance, appeared in 1902, to be superseded fifty years or so later by the benzodiazepines. The sulphonamides were introduced in 1935, followed by penicillin in 1942, the corticosteroids in 1952, and the phenothiazines in 1957. Since this era, the number of new chemical entities introduced into the practice of Western pharmacotherapy is virtually incalculable. Research and development of Western drugs was initially conducted mainly in academia. The first universities to study pharmacology as a discrete life science were in Dorpat, Estonia (1847) and Michigan, USA (1890). Schmiedeburg a student of another pioneer, Buchheim, now regarded as the true founder of Western pharmacology, published the first scientific text, Outline of Pharmacology in 1878. Abel researched adrenaline, histamine, and insulin during the period 1897 to 1926, and his student Reid-Hunt discovered acetyl choline in 1906. However, due to financial constraints, academia could no longer continue researching and developing new drug entities, and this eventually led to the formation of commercial companies dedicated to discovering, characterising and developing new pharmaceutical products. The pharmaceutical industry – ‘Big Pharma’ – was born in the 1930s.

**Basic theory:** Western synthetic drugs generally act to either stimulate or depress normal biochemical and physiological functions. They may act systemically and non-specifically upon all cells within the person’s body, as with chemotherapy. Alternatively, the drug may exert its effect locally in specific cells or tissues, or upon the affected organ alone, as with the proton pump inhibitors (Gaitonde BB et al., 2012). Furthermore, the drugs may exert their action on the surface of the cell, or on membranes, ion channels or other structures within the cell. They may also act by inhibiting key enzymes in a biochemical cascade within a membrane or organ which are essential for regulatory or metabolic performance. Pharmacological studies revealed that minute amounts of specific substances could have extensive effects on the body’s physiological systems, and slight changes in their chemical structure would result in radically different responses. The structure of the cell responsible for the effect was termed the receptor. This was viewed as a biological switch, activated or blocked by specific chemicals. Langley (1852-1926) originally introduced the concept of the drug receptor, visualising it as a switching mechanism which could be turned off and on by specific drugs. From this time onwards, many pharmacologists in various countries, such as Dale (1875-1968), Loewi (1873-1961), and Aihquist (1914-1983) were involved in the rapid progress of Western pharmacology. The receptor theory was the impetus to development of numerous drugs, which stimulate, inhibit or block these receptors as a prelude to pharmacological action. Western drugs have also been developed which inhibit the passage of electrolytes and neuro-hormones across cell membranes. The table (below) lists a selection of chemically based synthetic drugs based on the receptor theory:

**Table 2. Pharmacological action of Western drugs based on the receptor theory**

<table>
<thead>
<tr>
<th>Site</th>
<th>Action</th>
<th>Examples</th>
<th>Clinical usage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membrane receptor</td>
<td>Stimulation</td>
<td>Dopamine agonists</td>
<td>Treatment of Parkinson’s disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Beta agonists</td>
<td>Bronchodilators for asthma</td>
</tr>
<tr>
<td>Membrane receptor</td>
<td>Inhibition</td>
<td>Beta blockers</td>
<td>Lowering high blood pressure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anticholinergics</td>
<td>Treatment of mental disorders</td>
</tr>
<tr>
<td>Membrane receptor</td>
<td>Blockage</td>
<td>Serotonin re-uptake</td>
<td>Treatment of depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dopamine re-uptake</td>
<td>Anti-psychotic medication</td>
</tr>
<tr>
<td>Key enzymes</td>
<td>Inhibition</td>
<td>Angiotensin antagonists</td>
<td>Blood pressure reduction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proton pump inhibitors</td>
<td>Reduce stomach acid secretion</td>
</tr>
<tr>
<td>Membrane channels</td>
<td>Blockage</td>
<td>Calcium antagonists</td>
<td>Lowering of blood pressure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anaesthetics</td>
<td>Paralyse nerve transmission</td>
</tr>
</tbody>
</table>

As the body’s metabolic and physiological processes are highly complex, tightly regulated systems under the control of physis, interfering with a particular process may achieve a desired clinical outcome, but have unintended consequences elsewhere in the body. There is therefore no doubt that Western drugs based on the receptor theory will manifest as early side effects, later as adverse drug reactions, and
sometimes as toxic effects on, for instance, foetal development.

The unavoidable consequences of drugs based on the receptor theory, working against physis, are shown in the following examples:

A receptor inhibitor drug is the proton pump inhibitor, omeprazole – which opposes the cellular mechanism responsible for the production of gastric hydrochloric acid. By working against physis (as hydrochloric acid is necessary for digestion), food is incompletely digested, leading to side effects and complications, such as leaky gut syndrome, constipation, osteoporosis.

A receptor blocking drug is the beta blocker, atenolol. With age, inadequate diet and a poor lifestyle, a person’s blood circulation is compromised, resulting in a decrease in peripheral blood flow and an increase in blood pressure. Atenolol blocks the beta receptor site in the heart muscle. It also blocks beta receptor sites in other tissues and organs, resulting in side effects like bronchospasm, confusion and depression. The real underlying problem is not addressed, and other problems are created.

Stimulating drugs are dopamine agonists such as bromocriptine. In Parkinson’ disease there is a progressive loss of the neurotransmitter dopamine, so conventional treatment often involves administering a dopamine agonist. Side effects like hypotension, confusion and heart rhythm disturbances often ensue.

Safety of Tibb and other herbal remedies: There may be many different activities present in a single herb or, as with many herbal remedies, a combination of several herbs working in combination or synergistically for optimum effect (Firenzuoli F and Gori L, 2007); Bhikha R and Glynn J, 2018). Tibb philosophy is based on the undeniable understanding that physis is responsible for maintaining homeostasis between the many physiological and metabolic functions operating within and between the various body systems (Bhikha R and Haq A, 2000). With today’s technological advancements we know that these functions are carried out by various neurotransmitters, enzymes, hormones, cytokines and other signalling factors which communicate through receptor sites – all under the control of physis. Collectively they act holistically on several disorders, which may at times be seemingly unrelated to each other.

This can be illustrated by inspection of the medicinal plant Rauwolfia serpentina: Rauwolfia (Biradar et al., 2016). contains many different phytochemicals, including glycosides, flavonoids, tannins and alkaloids - of which more than 50 have been identified. When using the whole plant in the hypertensive patient, high blood pressure is effectively lowered by the major active alkaloid, reserpine. However, there are other alkaloids within the plant which also exert distinct pharmacological actions; adrenergic blocking activity (from ajmalicine), anti-arrhythmic activity (from chandrine), and hypnotic activity (from yohimbine). Moreover, the herb contains the alkaloid rauwolfine, which increases blood pressure - thus preventing blood pressure from dropping too low. When reserpine alone is used it is effective in reducing blood pressure. Unfortunately, there are several possibly side effects such as depression, nausea, headaches and dizziness. This has led to the use of reserpine being severely restricted in clinical use. If the whole plant is used, very few if any side effects result, highlighting the safety of using the whole plant as opposed to an isolated active ingredient. Whilst the above example highlights the side effect associated with a single isolated active ingredient from Rauwolfia serpentina, the same rationale may well apply to herbal supplements such as curcumin, which is an active ingredient in turmeric - obviously to a lesser extent.

Pharmacotherapy in Tibb: Pharmacotherapy in Tibb is intricately linked to its fundamental philosophical principles and is consistent with the temperamental and humoral theories (Bhikha R, 2018). Over the centuries, these principles have enabled Tibb practitioners to understand the nature, relevance and practice of aetiology, pathology, diagnosis and treatment. Tibb pharmacotherapy aims to (a) eliminate the causes; (b) normalise the humoral balance; and (c) restore qualitative harmony to tissues and organs. Whilst there have been numerous compilations of Tibb pharmacopeia’s over the past centuries, Volume 2 of Ibn Sina’s Canon of Medicine (Bakhtiar L, 1999) is still the most comprehensive. It describes more than 670 ingredients, mainly herbs, but also a number of animal and mineral ingredients. Staple foods such as grains, bread, milk, honey, dates and beans are also included. This volume highlights the following features:

Temperament: The temperament/quality of ingredients in Tibb is as important as their pharmacological actions (Chishti GM, 1991). For example, garlic, fenugreek and cinnamon are described as having Hot and Dry qualities. Coriander, borage, cardamom are Cold and Moist; basil and tamarind are Cold and Dry; and agrimony, ginger and black pepper are Hot and Moist.

Properties of drugs: Ibn Sina described the pharmacological action of specific drugs in relation to their physico-chemical properties, and their effect on humours (Bhikha R, 2017; Abu-Asab M et al., 2013). These include their potential for coagulation or dehydration, whether they are heavy or light, dense or tenuous, viscous or mucilaginous, oily or viscous, and also whether they are fragile in nature.

Degrees of activity: Ibn Sina categorised ingredients into four degrees of activity, or Orders, depending on their overall effect on the human body (Bakhtiar L., 1999). They take into account: (a) The potency of the substance’s pharmacological action; and (b) The intensity of the quality or temperament associated with the specific ingredient.

- **Ingredients in the first Order**: These include pharmacologically active foods (nutraceuticals) and dietary ingredients. They have only a minor pharmacological action but do contribute to health maintenance and the healing process e.g. quince, almonds, coconut.
- **Ingredients in the second Order**: Have a definite pharmacological action which is exerted as long as the active ingredient circulates in the bloodstream. Adverse effects may arise from these ingredients, especially in the elderly and children, e.g. agrimony, cinnamon and ginger.
- **Ingredients in the third Order**: Have the capacity to overwhelm the functions of the body. Large dosages
of products containing these ingredients can lead to serious side effects e.g. lobelia and artemisia.

- **Ingredients in the fourth Order**: Are highly potent, potentially toxic and possibly life-threatening, as they can either increase or decrease the functions of the body beyond the extent that supports life. Products containing these ingredients are always administered with other agents, which act to reduce their toxicity e.g. arsenic, opium and cannabis.

For the maintenance of health: Ingredients from the first Order and to a certain extent the second Order should be selected.

For the treatment of most conditions: Ingredients from the second and third Orders should be selected.

For the treatment of very serious conditions: Ingredients from the fourth Order may be selected, especially if the condition is potentially life threatening. However, they should not be used for extended periods.

**Differences between Tibb pharmacotherapy and other herbal medication**: In addition to addressing the qualitative and humoral imbalance associated with an illness condition, another important difference between Tibb pharmacotherapy and other disciplines is the temperament or quality of the medication. For example, the pharmacological action of *Commiphora mukul* is often included in common cold formulations, as it counteracts the specific symptoms of runny nose, fever/chills; however, it also has Hot and Dry qualities which oppose the Cold and Moist symptoms (Surendran S, 2018). This is a general rule in Tibb pharmacotherapy that the medication’s temperament/quality is opposite to the qualities associated with the condition (Bhikha R, 2018). In fact, the term ‘allopathic medicine’ (*allo*: Greek, opposite) originates from this understanding. That is, both the pharmacological action and temperament of the medication are important in relation to the clinical features associated with the ailment. This awareness of the medication’s temperament or quality in relation to the disease’s qualities is unique to Tibb herbal products. The Tibb approach therefore offers a rational approach to therapy. It logically and systematically describes the wide range of pharmacologically active drugs, whether derived from plant, animal or mineral sources. It includes (a) the drug’s action in redressing any qualitative/humoral imbalance underpinning the clinical disorder, and (b) the degree of effect, or potency, which it exerts. (Bhikha R and Glynn J, 2017)

**Differences between Tibb and western medication**: There are real, substantial and clinically important differences between Tibb pharmacotherapy and Western pharmaceutical drug treatment (Glynn J and Bhikha R, 2018; Rivera JO et al., 2013). The main features are:

- **Holistic approach**. Tibb embodies a holistic approach, based on the temperamental and humoral theories in its application of pharmacotherapy. The herbal remedy ingredients possess many active constituents (alkaloids, saponins etc.) which work at the cellular and humoral level, supporting, protecting and enhancing the body’s vital physiological and biochemical processes. Essentially, Tibb adopts a multi-targeted approach.

- **Natural form**. New-to-nature, synthetic chemicals, which comprise many Western drugs, have a specific but limited pharmacological action, which interferes with normal physiological and biochemical processes, so disturbing inner homeostasis. Tibb herbal remedies, on the other hand, act at three levels.

  - Firstly, they help to restore qualitative, humoral and temperamental balance, which has been upset during disease or disorders such as fatigue and IBS.
  
  - Secondly, they act pharmacologically on specific physiological and metabolic processes, by interaction with receptor mechanisms.
  
  - Thirdly, they regulate internal body processes, by working with physis. In doing so they enhance inner healing.

- **Spectrum of action**. Tibb herbal remedies, being based upon the whole plant, contain not only the active component, but also its precursors and its metabolites. These collectively ensure smooth pharmacological action and avoid excessive effects on basic metabolism. However, Western medication usually has a single, major effect, with little control exerted over the prevention of excessive action.

- **Multiple actions**. One agent alone may be able to attenuate specific symptoms in a disorder arising from a single cause, as many Western drugs successfully do. However, many disorders, especially those of a chronic nature, are the result of disharmony arising from multiple causes. In these cases, a herbal remedy with several different modes of action is more likely to be successful in ameliorating the symptoms of the disorder/s.

- **Side effects**. Because of the above differences, Tibb medication has a limited side effect profile compared to Western drugs.

**Combining Tibb medication with Western drugs**: For various reasons there has been a substantial increase in the consumption of herbal remedies in recent times (Ekor M, 2014). They are often combined with one another, and are commonly used simultaneously with Western drugs, taken for a wide range of acute, chronic and recurring disorders (Rivera JO et al., 2013). The interaction of herbs and drugs is only to be expected; if a herb triggers a pharmacological response, then it could conceivably interfere, to a greater or lesser extent, with a Western drug’s activity (Rao KK 2015). This has important ramifications for drug therapy, as many people are taking not one, but several, potent Western drugs. The potential for herb-drug interaction is therefore immense when the number of herbal products coming into popular use is considered (Izzo AA and Ernst E, 2001). The mechanisms by which a herbal product interferes with a drug, or vice versa, are not fully understood in most cases (Glynn J and Bhikha R, 2018). There are, however, a number of possible activities which explain the interaction; these are divided into pharmacokinetic and pharmacodynamic interactions.

**Pharmacokinetic Interaction** (Goodman and Gilman’s Manual, 2014; Palleria C et al., 2013)

**Inhibition of absorption**. The herb or drug acts on the other active agent to reduce or minimise its absorption. A number of agents have been identified:

- Pectins, resins, tannins may bind to certain antibiotics, preventing unimpeded absorption of the drug.
Garlic interacts with several drugs, by reducing their absorption into the body.

Enhancement of absorption: This is usually the result of increased gastric emptying or shorter gut transit time.

- Laxatives can increase these processes.
- Certain saponins can increase gastric emptying, so enhancing the rate of gastric emptying.

Increase in drug metabolism: The herbal product promotes an increase in metabolic enzymes in the liver, so boosting the breakdown or elimination of drugs.

- St John’s Wort reduces the plasma concentrations and increases clearance of a wide range of drugs.
- Echinacea affects the metabolic clearance of caffeine and certain anti-anxiety drugs.

Binding of drug by the herb component: Some antibiotics are chemically bound to certain botanical substances. This prevents or inhibits absorption through the intestinal wall, as the drug-herb complex is either too big to absorb, or too poorly soluble in the intestinal fluid.


Electrolyte depletion: Laxatives and diuretic drugs can reduce sodium and potassium levels in the body, and so lead to adverse cardiac effects.

The pharmacological effect is intensified: Certain herbs have specific pharmacological effects. If a drug is being co-administered, an additive or perhaps synergistic effect can arise.

- Hypoglycaemic drugs and herbal products used to treat diabetes may act together.
- Herbs which contain the alkaloids caffeine and ephedrine, or similar, may increase nerve stimulant drug action.

Summary

Despite the massive inroads made by modern Western medicine, herbal and natural therapies are experiencing a revival in usage, partly as a result of extensive research in their modes of action and clinical efficacy. Another notable reason for this renewed interest and increasing demand is due to the side effects often associated with Western medication. Western drugs exert their effects in only a limited number of ways. They stimulate, or inhibit, or otherwise interfere with the functioning of drug receptors; or reduce the activity of certain enzymes involved in key biochemical or metabolic processes; or they affect cell membrane permeability to certain ions. In contrast, herbal remedies differ in their mechanism of effect as they contain a wide range of active agents, their precursors and metabolites, which allow for close regulation of physiological and biochemical processes. Most herbal products have been around for millennia, and the efficacy of individual formulations has been established empirically by extensive clinical experience and observation. Whilst some of the pharmacological actions of herbal medicines have been clearly detailed and identified through time and tested use and recently through technological advancements; there are many others of which we only have an inkling of modes of action. Ibn Sina’s pharmacopoeia laid the foundations for Tibb pharmacology, allotting each herb to one of four categories, or orders, of clinical efficacy and patient safety. In addition, unique to Tibb as compared to other herbal remedies is the concept of qualities in relation to illness conditions. Tibb Pharmacotherapy makes available to the intricate wisdom of physis, many active constituents within herbal formulations, thereby allowing the body’s intrinsic healing ability to restore homeostasis at the temperamental and humoral level - ‘Treatment comes from outside; Healing comes from within’.

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