In the developed world, the use of herbs is undergoing a marked revival. Indeed, in many clinical practices, the use of St John's wort for depression, garlic for reducing elevated blood cholesterol and lipid levels, and Echinacea as a way of stimulating the immune system are virtually mainstream practice. Their regular use by practitioners of integrative medicine is well established. This awakening of interest and application of herbal medicine has gone hand in hand with investigations into the mechanisms by which various herbs exert their pharmacological effects.

Compared to herbal medicines, conventional drugs are relatively straightforward to investigate. This applies equally to both synthetic drugs, and to those derived from natural sources (mainly plants and fungi). Being single chemical entities they can be studied in strict isolation, as there is nothing in the drug’s dose form which can interfere to any significant extent with its pharmacological behaviour. By the time it reaches the market, the pharmacology of virtually every drug has been exhaustively researched, and the physiological response to it can generally be predicted with considerable accuracy. In addition, the drug’s dose levels for its target clinical indications can be precisely standardised. Moreover, any changes in the patient, such as improved clinical response or changes in physiological parameters, can be confidently attributed to the effect of the drug, by means of randomised clinical studies.

Herbal medicines, however, are a very different proposition. They consist (usually) of many compounds, each with separate, varying and distinct pharmacological activities. To the pharmacologist, the situation is unbelievably complex, and offers daunting challenges. Although considerable progress has been made over the last decade or so, the mechanisms of action of many, perhaps most, herbal medicines remains unclear. And even when they have been identified, often they do not fully explain the observed effects on the patient. A rich seam of pharmacological research beckons investigators.

Each component, although present in specific amounts, has a different pharmacological activity. But what distinguishes the effects of conventional drugs from herbal medicines is that there is invariably an interaction between the different components of the herbal medicine. One component often affects other active agents pharmacologically, perhaps exerting what has been termed a synergistic reaction.

What is meant by ‘synergy’? In healthcare, it means that the effect of combined treatment is more than the sum of each component’s individual effects. In the herbal medicine context, however, it refers to the idea that certain components in a plant extract can improve the therapeutic effect of active agents in the patient. One herb can enhance the effect of another given at the same time. It can also mean that the combined effect of a number of herbal components is actually greater than the sum of each of the individual components.
It is an important concept, as the practice of herbal medicine often entails the combination of several herbs in a thoughtful, rational and systematic way. When herbs are combined, the resulting effect is generally more powerful than when the herbs are taken alone. This is usually based on extensive experience and observation going back many years. The desired outcome, ultimately, is improved patient benefit.

A good example is the use of goldenseal, an herb used traditionally to deal with skin infections. One of its active components is the alkaloid berberine, which has been isolated and shown to possess rather weak antibacterial activity. However, this is increased greatly by (at least) three other substances in the plant – which themselves have virtually no antimicrobial activity. These inactive substances potentiate berberine, so leading to a much improved antibacterial effect\(^6\).

### Examples of Herbal Synergies

- When the herbal ginger extract is used the anti-ulcer effect is sixty-six times more effective than the active agent, zingerberene, when isolated and used alone\(^7\).
- The bioavailability of vitamin C present in many plants is improved when bioflavonoids like rutin are present\(^7\).
- Herbal treatment for infertility improves considerably if knotgrass is added, although knotgrass itself has little activity in this disorder\(^8\).
- Synergy shown by Echinacea – two types added together give x3 effect, not x2 effect\(^9\).
- The sedative herb valerian, at a dose of 60mg, when given with hops (40mg), is pharmacologically equivalent to 400mg valerian alone\(^3\). This combination benefits the user greatly, as valerian alone can cause stomach pain at the higher dose.
- Goldenseal, used for skin infections, contains berberine, which isolated has only weak antibacterial activity. This is potentiated by other substances in the plant, which are inactive themselves\(^6\).

The meaning of synergy has now been broadened somewhat. Like the words ‘holism’ and ‘quantum’, the original meaning has been extended to include other related concepts. Synergy is now used to describe the effect of one herb in improving the effect of another. For example, use of the laxative senna can lead to stomach cramps in some people. If ginger is taken simultaneously, then these cramps are avoided, or at least minimised\(^10\).

A further meaning of synergy relates to the simultaneous use of herbs with other contributors to healthcare. One aspect of this is becoming increasingly important – combining herbal therapy with adjustment to lifestyle\(^1\). As the cost of healthcare escalates, bringing in lifestyle changes is a very cost-effective way of increasing the probability of a successful therapeutic outcome. This means, for example, that herbal therapy for joint pains will be much effective when combined with a specific diet or mild form of exercise. Also, an asthmatic patient will benefit far more when herbal therapy is combined with breathing exercises, chest massage and improved sleep hygiene.

How does synergy operate? In many cases, the mechanism cannot yet be satisfactorily explained. It is likely that each case is different. There are two main processes by which synergy manifests. First, there may be *pharmacokinetic interaction* between the different herbs present in the formulation\(^5\). This involves interaction between herbal components in terms of absorption, distribution, metabolism and elimination (or excretion). One herbal component may improve absorption and bioavailability of a second, by increasing gastric emptying, for instance. Another may increase the blood level of an active component by attaching to binding sites on blood albumin, so displacing it, so leading to more a higher concentration of the free form\(^5\).
The second main synergistic process is pharmacodynamic interaction. This occurs, for example, when several components in the herbal medicine compete for the same physiological system or receptor. This is often evident when two psychoactive herbs, such as valerian and kava, are given to a patient with anxiety. The response is likely to be markedly greater than the sum of the two given separately.\(^6\)

The synergistic effects of herbal medicines also extend to their treatment of complex disorders. Take hypertension for example. A person with hypertension is often affected by co-existing disorders like glucose intolerance or diabetes, abnormally high blood cholesterol/lipid levels, and perhaps heart problems. The reason is that there is unlikely to be just one cause for the disharmony which affects the person. Long term lifestyle, environmental or exposure to infective agents may be involved. Synergistic action in this clinical situation is very important, as the disorder is so severe or intractable that no single ingredient is likely to be sufficiently effective. A single drug may be very effective in reducing the elevated blood pressure, but is unlikely to deal effectively with the other disorders. An herbal medicine is more likely to achieve a beneficial effect based on the synergy of its components.

Combining herbs to achieve the best therapeutic effect is a skilled process. Fortunately, many of the herbal medicines’ fixed combination have been designed according to experience gained over many generations. This means that there is justifiable confidence in the outcome of treatment, without the likelihood of unpleasant surprises, such as an adverse event.

Finally, there is the cost factor. Ginseng is expensive, but when given in combination with ‘assisting herbs’ the duration of action is extended. The amount of ginseng used can be reduced significantly, with considerable cost savings.\(^8\)

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Conventional medicine accepts synergistic action when treating cancer, hypertension, HIV/Aids, bronchial asthma and infection.