Synergy- a key herbal concept
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Introduction
Plant medicines are ideal tools to restore health and treat disease because they consist of a multiplicity of chemical components that act synergistically to make active constituents bio-available or to buffer otherwise potentially powerful active principles, preventing adverse effects. In this way many medicinal herbs act like foods to restore disrupted physiological processes. The concept of synergy is utilised by herbalists in their use of individual herbal medicines in that a single medicinal plant contains an orchestra of chemicals working together within the body to maintain health and treat disease. The therapeutic effect of the whole plant tends to be significantly more effective than the particular action of its known constituents. In this context, two and two turns out to add up to rather more than four. Using this principle, herbalists customarily combine herbs to take further advantage of the synergistic healing potential of their plant medicines.

Polypharmacy
This key traditional therapeutic herbal strategy is often termed *polypharmacy* -the combining of several medicinal herbs to achieve extra therapeutic effectiveness. This stratagem is a fundamental feature of practically every traditional medicine system the world over. Traditional Chinese, Ayurvedic and Tibetan herbal formulae contain combinations of a dozen or more plant medicines and western herbalists (phytotherapists) also customarily combine several herbs together in individualised prescriptions. These combinations represent the distillation of hundreds of years of herbal experience.

Polypharmacy does not fit the medical model for developing conventional drugs. Most pharmaceutical research is designed to identify and validate a single chemical to treat a particular disease. Whilst it is true that around 120 current licensed drugs were originally derived from plant sources - e.g. aspirin from willow, steroids from the Mexican yam, digoxin from foxglove, theophylline from tea, morphine from the opium poppy [1] - nevertheless, the extracted isolated active is perceived as scientifically purified and assayed and is thus superior to its plant source. Plants are only valued by the pharmaceutical industry for their perceived “actives “;the remaining “inert” constituents are generally discarded.

Combination therapy
Ironically, the sceptical stance adopted by scientists to plant polypharmacy is contradicted by the common practice of combining drugs to treat a wide range of serious diseases like HIV, AIDS, TB, malaria, diabetes, hypertension, MRSA etc. Pharmacologists now acknowledge that the individual actions of one drug are subject to modification by a second drug and that multi-drug regimens (“*combination therapy*”) confers beneficial new actions that do not occur when using each drug on its own.[2] It has thus been established that combination drug therapy can deliver greater therapeutic effect than can be achieved with a single conventional medicine. Moreover, it has become evident that combination therapy can attain the same

[1] Taylor L. Plant-based drugs and medicines. Article available at - http://chemistry.about.com/gi/dynamic/offsite.htm?site=http://www.rain%2Dtree.com/plantdrugs.htm.
[2] Toews ML, Bylund DB. Pharmacologic principles for combination therapy. *Proc Am Thorac Soc*. 2005;2(4):282-9; discussion 290-1. Review.

therapeutic effect as when using a single drug, but with fewer deleterious side effects.[3] Pharmacologists differentiate between two types of synergy, based on the nature of the interaction: *pharmacodynamic or pharmacokinetic*.

Pharmacodynamic synergy

This results from the enhancement of action when two drugs are directed at a similar receptor target or physiological system. A herbal example of this process can be seen in the consituents of senna, Sennocide A and Sennocide C. Separately these have a similar laxative action but a mixture of these two compounds in the ration 7:3 (which is more or less the naturally occuring ratio found in senna) all but doubles the laxative effect.[4]

Pharmacokinetic synergy

This results from alteration of the processes of drug absorption, distribution, biotransformation (metabolism), or elimination. An example of pharmacokinetic synergy is the simultaneous ingestion of vitamin C to improve the absorption of iron.[5] For this reason, many herbs rich in iron and vitamin C such as nettles or watercress combat iron-deficiency anaemia. On the other hand because of its tannin content, drinking tea at mealtimes may inhibit iron as well zinc and copper absorption by decreasing their bioavailability[6]. Other pharmacokinetic interactions may also result in unwanted effects. Both grapefruit juice and St John's wort exert a significant but contrary effect on an enzyme system on the liver (Cytochrome P450) that is responsible for metabolizing a range of drugs. Grapefruit is a potent inhibitor of Cytochrome P450, slowing the metabolism of many drugs to about half the normal rate. St John's wort markedly induces (i.e. accelerates) the metabolic breakdown of many conventional drugs. For this reason, patients taking the anticoagulant warfarin should not take St John's wort at the same time as the speed at which warfarin is washed out of the system is accelerated by the herb.

Ancient knowledge

The development of pharmacodynamic and pharmacokinetic insights is a relatively new pharmacological development but knowledge of plant interactions on this basis goes back thousands of years. For example, pharmacodynamic interactions were systematically documented in Oriental medicine. The additive effect is generally referred to as mutual accentuation (*Xiang Xu*), or mutual enhancement (*Xiang Shi*). An example is the combination of Gypsum and Rhizoma Anemarrhenae to clear toxins. On the other hand, an antagonistic effect is referred to as mutual counteraction (*Xiang Wei*), mutual suppression (*Xiang Sha*), or mutual antagonism (*Xiang Wu*). Chinese herbal texts issue a warning about combining tea with ginseng as tea is said to reduce the effect of this famous Chinese tonic.[7].

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[3] Reid JL. Pharmacokinetic and pharmacodynamic aspects of the choice of components of combination therapy. *J Hum Hypertens* 1995;9:S19–S23

[4] Kisa K, Sasaki K, Yamauchi K, Kuwano S. Potentiating effect of sennoside C on purgative activity of sennoside A in mice. *Planta Med.* 1981 Jul;42(3):302-3.

[5] Teucher B, Olivares M, Cori H.. Enhancers of iron absorption: ascorbic acid and other organic acids. *Int J Vitam Nutr Res*. 2004 Nov;74(6):403-19.

[6] Pizarro F, Olivares M, Hertrampf E, Walter T.Factors which modify the nutritional state of iron: tannin content of herbal teas. *Arch Latinoam Nutr*. 1994 Dec;44(4):277-80.

[7] Bensky D, Gamble A. *Chinese herbal medicine material medica* revised edition. Eastland Press 1986.