Pharmacognosy

Third Year/Second Semester

Lecture one

Phytotherapy

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This Lecture will cover the following topics.

1. Phytotherapy and Introduction
2. Important Definitions
    - Traditional Medicine
    - Complementary and Alternative Medicine
    - Integrative Health
    - Homeopathy
    - Medical Herbalism
    - Aromatherapy
3. Differences Between Homeopathic and Herbal Medicine
4. Differences Between Phytotherapy and Herbalism
5. Role of Pharmacist in Patient Education
6. Sample Questions

References:

1. National Center for Complementary and Alternative Medicine. Available at: http://nccam.nih.gov. Accessed on February 8, 2005
2. Michael Heinrich, Joanne Barnes, Simon Gibbons, Elizabeth M. Williamson" Fundamentals of Pharmacognosy and Phytotherapy" Second Edition, Churchill Livingstone, Elsevier 2012.
3. Sarfaraj Hussain "Patient Counselling About Herbal-Drug Interactions" Afr J Tradit Complement Altern Med. (2011) 8(S):153-163
4. Ufuoma S Ahwinahwii and Evans K Attakuiu "Factors affecting availability and use of herbal medicines by community pharmacist" Journal of Science and Practice of Pharmacy December 2015; 2 (1): 18-22

1. Phytotherapy

Phytotherapy is a science-based, empirical approach to using medicinal plants in the treatment and prevention of disease.

In the upcoming lectures we will discuss the use of different remedies in the treatment of different diseases and symptoms. The aim of these lectures is to provide a scientific basis for the use of plants in pharmacy (pharmacognosy) and also to describe the main characteristics of herbal medicines (herbal medicinal products, herbal remedies, phytomedicines) and their clinical uses.

1.1. Introduction

All modern medicine is derived originally from ancient herbal traditions. These have evolved to produce the conventional medicine known in the West, which uses both synthetic drugs and isolated natural compounds.

Plant extracts are now rarely used by physicians or in hospitals, although herbal remedies are popular with the public and improvements in their formulation have resulted in a new generation of phytomedicines that are more potent than before and also chemically standardized. There is, however, a resurgence of interest in the older Oriental systems; this is due partly to dissatisfaction with conventional treatments and partly to the constantly growing interest in all things natural, environmentally friendly and biodegradable.

Other reasons for the increased use of herbal medicines may range from the appeal of products from 'nature' and the perception that such products are 'safe' (or at least 'safer' than conventional medicines, which are often referred to as 'drugs'), to more complex reasons related to the philosophical views and religious beliefs of individuals.

Whether or not pharmacists, doctors and other healthcare professionals accept the validity of these older medical systems, it is necessary for them to know about their basic principles for two main reasons. First, to be able to advise patients who may wish to consult an alternative practitioner and, second, because traditional use is a common starting point in the ongoing search for new drugs.

2. Types of Drugs Derived from Plants

In general, there are three types of herbal products:

a) Herbal drugs derived from specific parts of medicinal plants.

Botanical drugs which form the basis for herbal remedies or phytomedicines, for example:

- The leaves of Ginkgo biloba, used for cognitive deficiencies (often in the elderly), including impairment of memory and affective symptoms such as anxiety.
- The flower heads of chamomile (*Chamomilla recutita*), used for mild gastrointestinal complaints and as an anti-inflammatory agent.

b) Natural compounds isolated from nature.

These are pure chemical entities, often used in the form of licensed medicines. They are sometimes produced synthetically and referred to as 'nature identical' (if that is the case) but were originally discovered from plant drugs. Examples include:

- Morphine, from opium poppy (*Papaver somniferum*), used as an analgesic.
- Digoxin and other digitalis glycosides, from foxglove (Digitalis spp.), used to treat heart failure.

c) Nutraceuticals or functional food

Nutraceutical may be defined as "a food (or a portion of a food) that essentially provides distinct health and medical benefits, even including the prevention and or treatment of a particular disease.

Many foods are known to have beneficial effects on health. Examples include:

- Garlic, ginger, turmeric and many other herbs and spices
- Anthocyanin- or flavonoid-containing plants such as bilberries, cocoa and red wine

3. Definitions

- **Traditional Medicine (TM)**

Traditional medicine can be defined as: Medical practice that includes diagnosis, prevention and treatment, relying on practical experience and observations handed down from generation to generation, whether verbally or in writing.

Several types of traditional medicine have been used as: Traditional Chinese Medicine (TCM), Ayurveda, Traditional African medicine (TAM) or Traditional African medical systems (TAMS), each of these systems has its own concept and base of treatment.

- **Complementary and Alternative Medicine (CAM)**

Complementary and alternative medicine (CAM) are defined by the National Center for Complementary and Alternative Medicine (NCCAM), as "health care approaches with a history of use or origins outside of mainstream medicine.

NCCAM applies the term to a broad spectrum of practices, distinctions exist among the various approaches as:

a) Complementary: use of a nonmainstream approach together with conventional medicine
b) Alternative: use of a nonmainstream approach in place of conventional medicine
c) Traditional: cultural healing systems that have persisted for thousands of years.
d) Integrative: integration of nonmainstream practices into conventional medical treatment and health promotion.

- **Integrative Health (National center for complementary and integrative health NCCIH)**

Integrative health care often brings conventional and complementary approaches together in a coordinated way. It emphasizes a holistic, patient-focused approach to health care and wellness—often including mental, emotional, functional, spiritual, social, and community aspects—and treating the whole person rather than, for example, one organ system. It aims for well-coordinated care between different providers and institutions.

Example: integrative Approaches for Symptom Management in Cancer Patients:

Cancer treatment centers with integrative health care programs may offer services such as acupuncture and meditation to help manage symptoms and side effects for patients who are receiving conventional cancer treatment. Although research on the potential value of these integrative programs is in its early stages, some studies have had promising results.

Please see this video for meditation

https://www.youtube.com/watch?v=inpok4MKVLM

For example, NCCIH-funded research has suggested that:

a. Massage therapy may lead to short-term improvements in pain and mood in patients with advanced cancer.

b. Yoga may relieve the persistent fatigue that some women experience after breast cancer treatment, according to the results of a preliminary study.

c. Tai chi and Qi Gong have shown promise for managing symptoms such as fatigue, sleep difficulty, and depression in cancer survivors.

https://www.youtube.com/watch?v=rLxiO0zFaNo

- **Homeopathy**

The name homeopathy, coined by its originator Samuel Hahnemann, is derived from the Greek words for 'similar suffering' referring to the 'like cures like' thus a substance which can cause symptoms if taken in large doses, can be used in minute doses to treat similar symptoms; Thus, it is based on two theories:

a. "Like cures like"—the notion that a disease can be cured by a substance that produces similar symptoms in healthy people.

b. "Law of minimum dose"—the notion that the lower the dose of the medication, the greater its effectiveness.

Example: Digitalis in high doses causes arrhythmias, but this drug is used routinely in low doses to treat this condition.

Another example small doses of allergens such as pollen are used to de-sensitise allergic patients.

- **Medical Herbalism:**

Is the use of herbs in the treatment of various disease based on traditional knowledge, in addition to patient's psychological and emotional wellbeing, as well as physical health. Herbalists select herbs on an individual basis for each patient (in line with the holistic approach), thus it is likely that even patients with the same physical symptoms will receive different combinations of herbs.

- **Aromatherapy**

Aromatherapy is the therapeutic use of essential oils. These are obtained from plant material (e.g. roots, leaves, flowers, seeds) usually by distillation, although physical expression (using compression and pressure) is the method used to obtain some essential oils, mainly those from the skin of citrus fruits.

3.1. Differences Between Homeopathic and Herbal Medicine

Homeopathic remedies and herbal medicines are often confused and/or deemed to be similar.

The fundamental differences between the two types of preparation are:

- Homeopathic remedies are (mostly) highly dilute, whereas herbal medicines are used at material strengths. However, since homeopathic preparations are first extracted from, for example, plant material and then diluted, there is a borderline group including mother tinctures and lower potencies (i.e., less diluted), which still may contain biomedically relevant amounts of active ingredients.
- Many homeopathic remedies (around 65%) originate from plants, whereas by definition, all herbal medicines originate from plants (for example, plant-based homeopathic preparations. Many species used for preparing homeopathic remedies have a history of medicinal use; others are poisonous

if undiluted. Other materials used to prepare homeopathic remedies include animal, insect, biological, drug, chemical, and mineral.

3.2. Differences between Phytotherapy and Herbalism.

There are distinct differences between Phytotherapy and Herbalism, summarized by the following points and tabulated in Table (1)

- Importantly, the herbalist's approach has not been evaluated in controlled clinical trials, whereas there are numerous controlled clinical trials of specific Phyto-therapeutic preparations.
- Another vital difference is that, although many of the same medicinal plants are used in each of the two approaches, the formulations of those herbs are often very different. For example, herbalists use St John's wort (Hypericum perforatum L.) in rational Phytotherapy. However, in rational Phytotherapy, the preparations will likely be extracts of *H. perforatum* herb (leaves and tops) standardized on hypericin content and formulated as tablets. By contrast, herbalists are likely to use a tincture of *H. perforatum* herb that is not standardized on its content of any constituent.

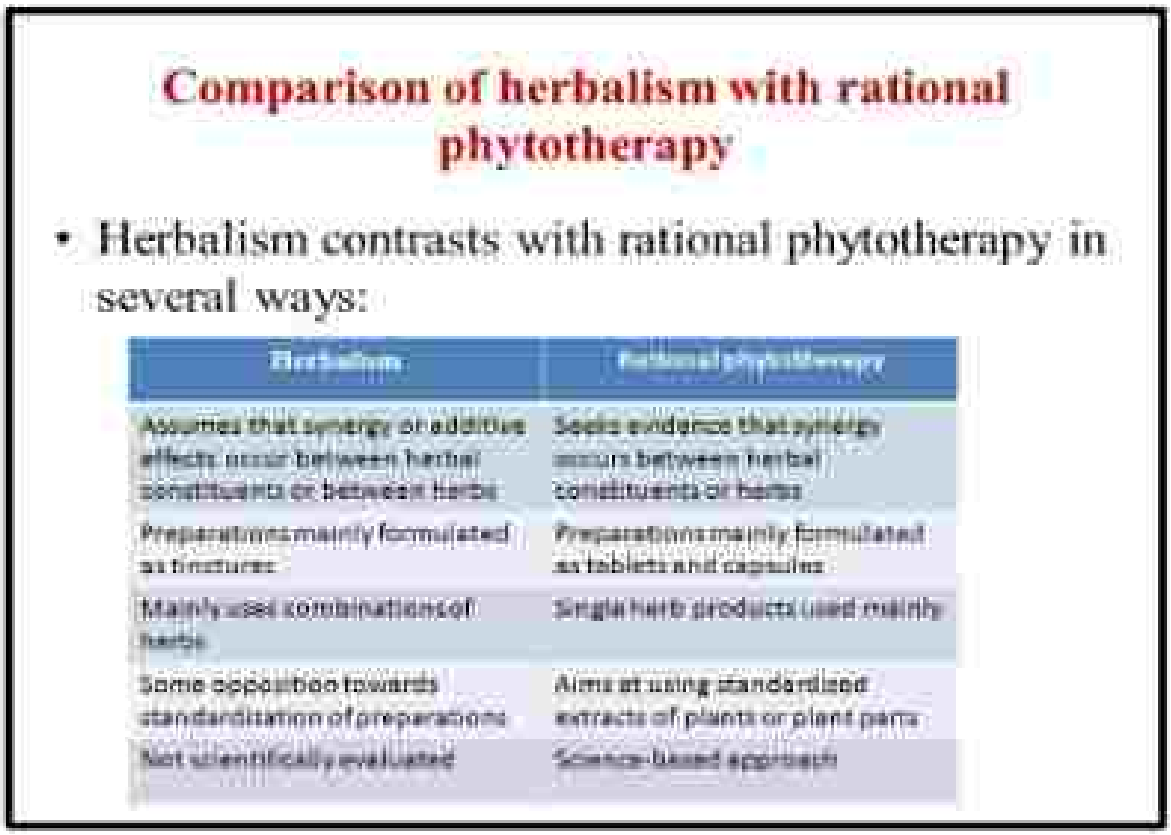

Table 1" Comparison of Herbalism with Rational Phytotherapy"

4. Role of Pharmacist in Patient Education

Most herbal products can be sold or supplied without the involvement of a healthcare professional, and several studies have confirmed that many individuals do not seek professional advice before purchasing or using such products, even when purchased from a pharmacy, which puts the patient at risk of possible drug herbal interactions and other more complicated issues.

Pharmacists are primary health providers and are expected to give guidance to their patients on the use of medicines. These include herbal medicines, now commonly sold as Over–the–counterdrugs. They should hold the responsibility to deliver effective, safe, quality medicines and services to achieve optimal health outcomes, providing the patients with assistance on how to take a drug dose,

preparing and dispensing medications, and reminding them to take medicines and re-dispensing and follow-up of patients to identify difficulties in the use of drugs.

Many issues regarding the safety of co-administration of these products and conventional medicines must be highlighted. Potential herb-drug interactions can be avoided by prescribing them so that they do not result in any unwanted pharmacokinetic interaction or by reducing the dose in case both the herb and the pharmaceutical drug have the same therapeutic action (e.g., sedatives and hypoglycemic agents). Those who are elderly, debilitated, or receiving polypharmacy are more at risk for an herb-drug interaction, and particular attention is required in these cases.

For patients using CAM, the physician needs to know more about the mechanism of action of drugs and herbs. An effective educational intervention could bridge this gap between acceptance and knowledge about CAM.

Unfortunately, many people mistakenly assume that all herbs and foods are safe because they are natural; this is not so. Very often, herbs and foods may interact with medications you normally take and result in serious reactions.

Herbs and drugs may interact either pharmacokinetically or pharmacodynamically. The predominant mechanism for this interaction is the inhibition of cytochrome P–450 3A4 in the small intestine, resulting in a significant reduction of drug pre-systemic metabolism. An additional mechanism is the inhibition of P glycoprotein, a transporter that carries drug from the enterocyte back to the gut lumen, result in a further increase in the fraction of drug absorbed.

Other herbs may have the potential to induce the CYP450 enzyme system. Perhaps the most notable is St. John's Wort (*Hypericum perforatum*), which reduces the plasma concentration of many drugs such as amitriptyline, digoxin, theophylline, non-steroidal anti-inflammatories (NSAIDs), and oral contraceptive pills.

Moreover, serious adverse effects have been encountered with warfarin due to herb-based inhibition of its metabolizing enzymes.

Thus, it is crucial that during medication reconciliation, pharmacists determine whether patients use or intend to use CAM. This includes herbal supplements. Assessing patients' knowledge of their health status, diseases, and treatments is important. Identify any potential interactions of drugs and herbal remedies and document them in the medical record; then follow up with the patient and provider as indicated. It is also essential to consider a patient's economic constraints and cultural preferences and educate patients about making informed choices. Evaluate their understanding of the difference between OTC "drugs" and "food supplements," such as unregulated herbs provided in tablet or capsule form that lack FDA approval.

It is also imperative to caution patients about the potential for fraudulent advertising, especially on the Internet, and warn patients that advertisers who lack scientific data to support their claims often use user testimonials. Moreover, it is necessary to encourage patients to disclose their CAM supplement use to their healthcare providers fully.

Table 2 represents some Herbal-Drug interactions.

Herbal drugs	Biological source	Interaction reported or suspected with Ref
Ginkgo	*Ginkgo biloba*	Concurrent use of ginkgo and nonsteroidal Anti-inflammatory agents may result in an increased risk of bleeding, and warfarin causes bleeding
Garlic	*Allium sativum*	Concurrent use of garlic and anticoagulants results in an increased risk of bleeding
Ginger	*Zingiber officinale*	Concurrent use of ginger and anticoagulants may result in an increased risk of bleeding, sulfa guanidine enhances absorption
Ginseng	*Panax ginseng*	Concurrent use of ginseng and antidiabetic agents may result in increased risk of hypoglycaemia
St John's wort	*Hypericum perforatum*	Concurrent use of digoxin and St John's wort may reduce digoxin efficacy
St John's wort	Hypericum perforatum	Warfarin (cause bleeding), serotonin-uptake inhibitors (cause mild serotonin syndrome), indinavir (decreased bioavailability), digitoxin, theophylline, cyclosporin, phenprocoumon, and oral contraceptives reduce bioavailability
Rhubarb	*Rheum officinale*	Cardiac glycosides and anti-arrhythmic agents potentiate by reducing potassium via laxative effect
Astragalus	*Astragalus membranaceus*	Cyclosporine, azathioprine, methotrexate impair immunosuppressive effects
Licorice	*Glycyrrhiza uralensis*	Corticosteroids and thiazide diuretics potentiating digitalis or other cardiac glycosides increase sensitivity
Ma-huang	*Ephedra sinica*	MAO inhibitors cause hypertension, cardiac glycosides or halothane react to produce cardiac arrhythmia, caffeine intensify cardiovascular side effects
Aloe	*Aloe ferox*	Cardiac glycosides and antiarrhythmic agents potentiate by reducing potassium via a laxative effect
Salvia	*Salvia miltiorrhiza*	Warfarin causes bleeding
Bupleurum	*Bupleurum falcatum*	With sedatives potentiating effect

Table 2 "Important Drug-Herbal Interactions"

Below are some references that you may refer to for drug interaction or information about a specific herbal product.

- https://reference.medscape.com/drug-interactionchecker
- https://www.stonybrookmedicine.edu/sites/default/files/herbal_medicines_interactions-1.pdf
- https://www.nccih.nih.gov/health/providers/digest/herb-drug-interactions

5. Remedies used in the treatment of the Cardiovascular system.

Cardiovascular (CV) disorders are responsible for many deaths in the Western world and are a consequence of lifestyle and diet, as well as being hereditary to some extent. Severe conditions such as heart failure should be treated only under the guidance of a qualified physician. Still, some minor forms of CV disease respond well to changes in diet, taking more exercise, and Phytotherapy.

5.1. Circulatory disorder.

Circulatory disorders improve from several pharmacological effects, particularly those involving anti-inflammatory and antioxidant activity. Plant drugs with these actions are important in treating hemorrhoids, varicose veins, impaired visual acuity, and even memory enhancement when blood flow to the brain may be affected.

They usually contain saponins with anti-inflammatory activity or anthocyanidins and other antioxidants. The most important are bilberry, butcher's broom, horse chestnut, ginkgo and garlic.

- **Bilberry**

The bilberry, also known as the huckleberry or blueberry (*Vaccinium myrtillus* L., Vacciniaceae (figure 1)), is used medicinally both as the ripe fruit and as the leaves.

The fruit contains Anthocyanosides, mainly galactosides and glucosides of cyanidin, delphidin, and malvidin (figure 2), and vitamin C and volatile flavor components. The berries were traditionally used as an antidiabetic, astringent, and antiseptic for diarrhea. However, bilberry is now more important as an agent to improve blood circulation in venous insufficiency, especially for vision disorders such as retinopathy caused by diabetes or hypertension.

Anthocyanosides are mainly responsible for these properties due to their antioxidant and free radical scavenging properties. Other cardiovascular benefits include antiplatelet and anti-atherosclerotic effects.

The usual daily dose of a standardized Anthocyanosides bilberry extract is 480 mg, taken in divided doses (figure 3). Few side effects have been observed, as would be expected of a widely consumed food substance.

Figure 1 "*Vaccinium myrtillus*"

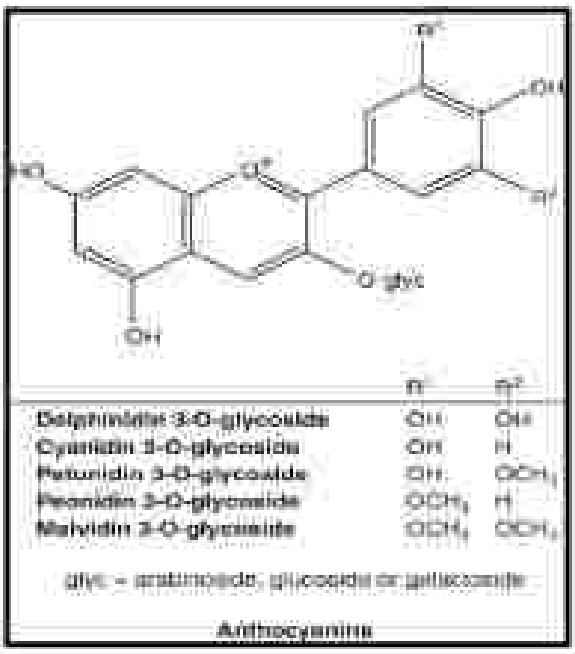

Figure 2 "Anthocyanin structures"

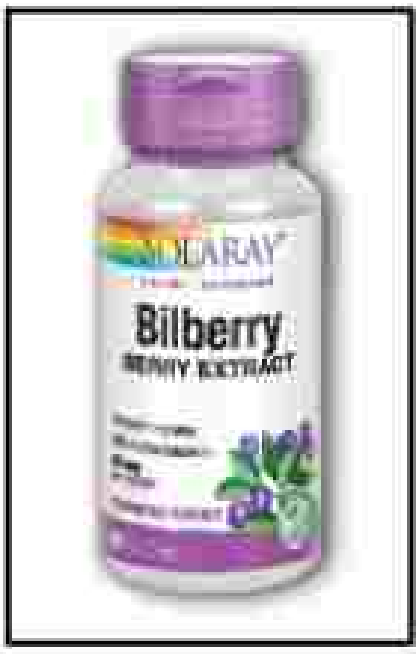

Figure 3 "The pharmaceutical product of Bilberry

- **Ginkgo**

Ginkgo biloba, a member of the Family Ginkgoaceae (Figure 4), can also be used in cases of peripheral arterial occlusive disease and other circulatory disorders.

Although probably less potent than some synthetic drugs, it has the advantage of being well tolerated. Ginkgo improves blood circulation and can alleviate some symptoms of tinnitus, intermittent claudication, and altitude sickness. Ginkgo also has an antiplatelet activity.

Ginkgo leaf extracts contain phenolic acids, Proanthocyanidins, flavonoids (such as myricetin, kaempferol, isorhamnetin , and quercetin), terpenes, flavones, and alkylphenols.

Ginkgo is found in many pharmaceutical products (figure 5), and the usual daily dose is 120–160 mg of extract.

Figure 4 "Ginkgo biloba"

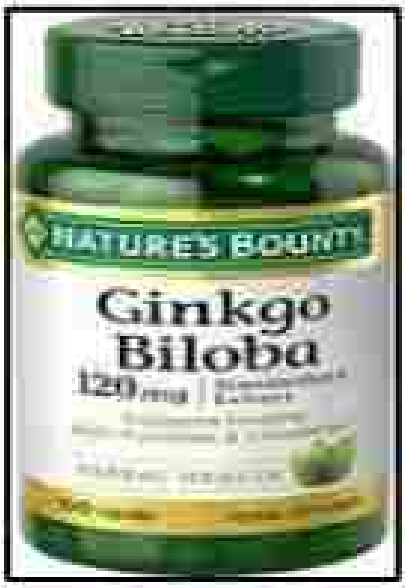

Figure 5 "Pharmaceutical product of Ginkgo"

- **Red Vine Leave**

Certain varieties of grapevine (*Vitis vinifera* L. F. Vitaceae (figure 6)) produce red leaves, which are used to treat CVI (Chronic venous insufficiency) and, in particular, varicose veins.

Grape leaves contain a wide range of polyphenols, including quercetin-3-O-beta-D-glucuronide (figure 7) and iso-quercitrin (the main flavonoids),

anthocyanins, oligomeric Proanthocyanidins, catechin, epicatechin monomers and dimers, gallic acid and astilbine.

Clinical studies have shown that the extract can improve objective symptoms of CVI and may prevent further CVI deterioration. Red vine leaf extracts also improve microcirculation and aid wound healing. In vitro, studies indicate that they have antioxidant and anti-inflammatory properties they inhibit platelet aggregation and hyaluronidase and reduce edema, possibly by reducing capillary permeability. Preclinical in vivo experiments demonstrated anti-inflammatory and capillary wall thickening effects.

Commercial products are usually standardized to 90% polyphenols and 5% astilbine, with a daily dose of 360 mg of red vine leaf extract being the recommended internal dose (figure 1.7.2.8).

Figure 6 "Red Vine Leaves"

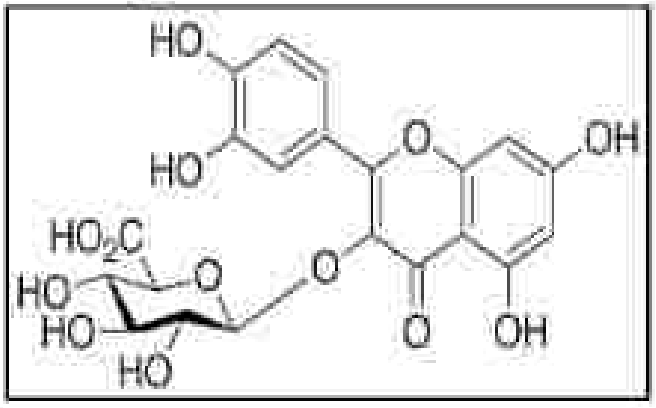

Figure 7 "quercetin-3-O-beta-D-glucuronide structure"

Figure 8 "Pharmaceutical products of Red Vine Leaves"

5.2. Antiplatelet and atherosclerotic drug

Thrombosis and atherosclerosis are the result of a sedentary lifestyle and high sugar and fat consumption. Their incidence is rising, and the age at which patients show signs of these conditions is getting younger. These conditions are closely related in that atherosclerosis predisposes to thrombus formation and can result in peripheral arterial disease, myocardial infarction, and stroke. In addition to improving diet and regular exercise, preventative drugs can be taken, many of which are natural products of some kind.

Antiplatelet drugs are used prophylactically to decrease platelet aggregation and inhibit thrombosis. The standard antiplatelet drug is aspirin, used in lower doses (75–300 mg daily) than for pain relief (300 mg to 1 g, up to four times daily).

Two examples in this group: garlic and Ginkgo (Ginkgo has been discussed earlier)

- **Garlic**

The garlic bulb (*Allium sativum*, Liliaceae (figure 9) is composed of several small bulbs or 'cloves', covered with papery, creamy-white bracts.

Garlic contains a large number of sulfur compounds which are responsible for the flavor and odor of garlic, as well as its medicinal effects. The main compound in the fresh plant is alliin, which, on crushing, undergoes enzymatic hydrolysis by alliinase to produce allicin (figure10).

Figure 9 "Garlic Bulbs"

Different types of garlic preparations are available (figure11), such as standardized allicin-rich extracts, aged garlic extracts (particularly in the Far East) and capsules containing the oil (older products). All have different compositions, but it is recognized that the sulfur-containing compounds must be present for the therapeutic effect.

Garlic extract has been observed in animals with hypolipidemic activity, which has been attributed to S-allylcysteine, which is regarded as important in this activity. S-allylcysteine inhibits NF-kB synthesis and low-density lipoprotein (LDL) oxidation, which are both implicated in atherosclerosis.

Cardiovascular benefits are supported by the antithrombotic activity, shown in several studies, and an antiplatelet effect demonstrated by aged garlic extracts in

humans. Other health benefits of garlic are antibacterial, antiviral and antifungal effects, and, more importantly, chemo-preventative activity against carcinogenesis in various experimental models.

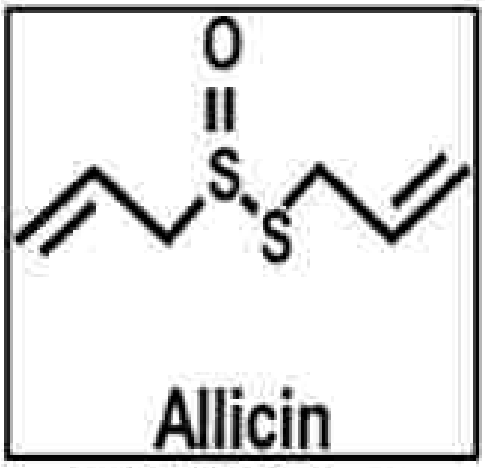

Figure 10 "Allicin Structure"

Figure 11 " Garlic Pharmaceutical Products"

6. Practice Questions

- Define Phytotherapy, Homeopathy and CAM
- Differentiate between Phytotherapy and Herbalism
- Explain the role of the Pharmacist in Patient education.
- Give an example of an herbal product (nutraceutical)that can be used to aid in managing Atherosclerosis.

THE END