Complementary and Alternative medicine

PHG 323 (*Phytotherapy*)

Part 2

Department of Pharmacognosy – College of Pharmacy - KSU

Side Effects / Toxic Reactions to Herbal Medicines:

Herbal medicines may show toxicity/side effects due to:

1) **Intentional addition of synthetic additives (e.g. adulteration of herbal remedies used for arthritis with synthetic anti-inflammatory drugs such as indomethacin).**

2) **Contamination with microorganisms or their toxins:**

- **Aflatoxins are mycotoxins produced by many *Aspergillus* species**
- **Aflatoxins are among the most carcinogenic substances known affecting the whole body, particularly liver and kidney.**

3) **Some herbal medicines were proved to be hepatotoxic due to their content of pyrrolizidine alkaloids**

4) Excessive ingestion or high doses:

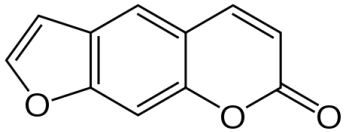
- **Excessive ingestion of Liquorice has resulted in typical side effects of corticosteroid type e.g. edema (salt and water retention) and hypertension.**

5) Hypersensitivity reactions:

- **Some herbs of family Asteraceae (e.g Chamomile) contain sesquiterpene lactones and possess allergic properties.**

6) Phototoxic reactions:

- **Some herbs of family Apiaceae (e.g. Parsley) contains furanocoumarins and cause phototoxic reactions and skin rashes.**



Phytotherapy could be used in:

- Cardiovascular system problems
- Respiratory tract problems
- Gastrointestinal disorders
- Musculoskeletal disorders
- Nervous system disorders
- Urinary system disorders
- Reproductive system problems
- Endocrine system problems
- Natural skin care cosmetics
- Natural wound healing products

For treatment of these health problem, Phytotherapy can be integrated with suitable Diet & Life style

Cardiovascular System Diseases (CVDs)

- According to WHO, an estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths.
- CVDs are concerned with disorders of the heart and blood vessels

CVDs include:

I. Congestive heart failure (CHF)

II. Arteriosclerosis and Arterial Occlusion

III. Hypertension

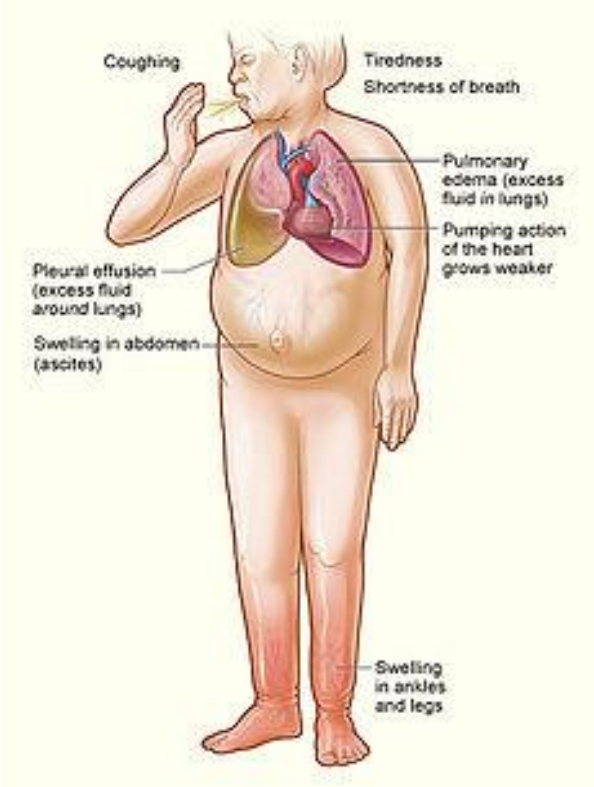
IV. Angina Pectoris

V. Cardiac Arrhythmias

VI. Chronic Venous Insufficiency

I. Congestive heart failure (CHF) فشل أو قصور القلب الاحتقاني

- This is one of the common causes of death particularly in old age.
- CHF occurs when the cardiac output is inadequate to provide the oxygen needed by the body.
- This results in:
  - Shortness of breath
  - Tiredness
  - Retention of salt and water
    → ankle swelling and
    pulmonary edema, etc.



Phytotherapy of CHF

- **Herbal medicines containing cardioactive glycosides (cardinolides or bufadienolides) are potentially useful.**
- **These drugs should be used under strict medical supervision due to their narrow therapeutic index.**
- **Examples**

Common (Latin) names	Part used	Key comp.	Dose/d
Foxglove (*Digitalis* spp.)	Leaves	Cardinolides	0.1 g
Kombe (*Strophanthus kombe*)	Seeds	Cardinolides	0.1 g
Squill (*Urginea maritima*)	Bulbs	Bufadienolides	0.1-0.5g

The cardiac glycosides act by:
Inhibition of Na^+/K^+ ATPase of cardiac cell membranes → intracellular **Na^+** concentration **increased** → transport of **Ca^{++} increased→ increase** in the systolic force of contraction **(+ve inotropic effect).**

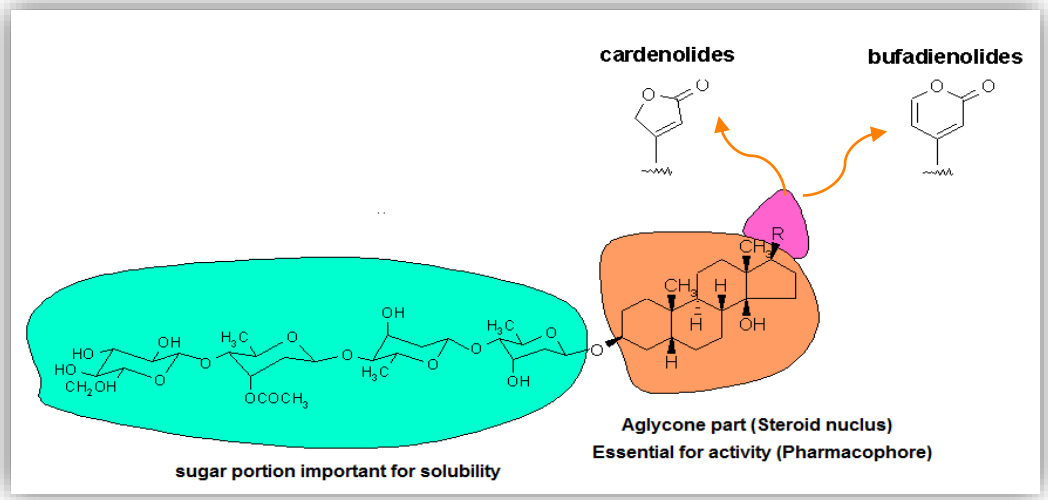
Illustrations

Herbal medicines of cardioactive glycosides and key constituents

Digitalis purpurea

Strophanthus kombe

Urginea maritima



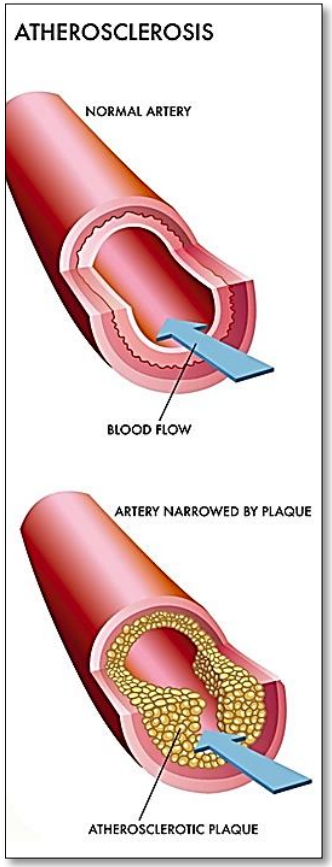
II. Atherosclerosis and Arterial Occlusion تصلب و انسداد الشرايين

- **Atherosclerosis is the hardening and narrowing of arteries which is caused by the buildup of fatty plaques and cholesterol in the artery**

- **Therefore, hyperlipidemia (abnormal high levels of plasma cholesterol and triglyceride levels) increases the risk of atherosclerosis and progression of arterial occlusion.**

- **Atherosclerosis is the usual cause of heart attacks, strokes, and peripheral vascular disease.**

- **Diabetes, smoking, hypertension, oxidative stress, and systemic infection are risk factors for atherosclerosis.**



Phytotherapy of Hyperlipidemia and Atherosclerosis

- **Several herbs are commonly used for decreasing low density lipoprotein (LDL) and hence they have a great significance in management of hyperlipidemia and related disorders.**

- **Examples**

Common (Latin) names	Part used	Key comp.	Dose/ d
Artichoke (*Cynara scolymus)*	Leaves	Caffeic acid deriv. (e.g. Cynarin) – flavonoids – sesquiterpene lactones	4-9 g
Garlic (*Allium sativum*)	Bulbs	Alliin → Allicin→ Ajoene	4 g
Fenugreek (*Trigonella foenum-graecum*)	Seeds	Steroid saponin – flavonoids - mucilage	6 g
Psyllium (*Plantago psyllium*)	Seeds	Mucilage - iridoids	15-40g

Illustrations

Herbal medicines of hyperlipidemia and Atherosclerosis

Garlic

Artichoke

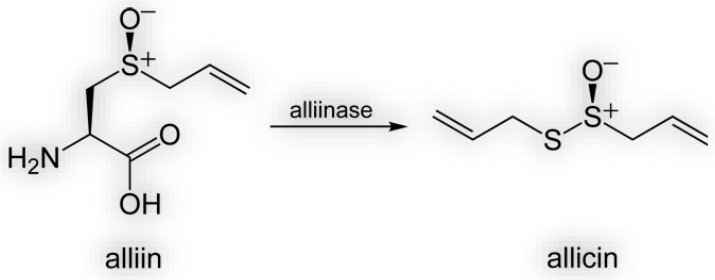
Ginseng

Fenugreek

Psyllium

a) Garlic (see also next lecture) الثوم

- The main constituent in garlic is **alliin** which on crushing will be converted by **alliinase** into **allicin**.



- Allicin is **odorous**, unstable and spontaneously degraded into a variety of **organosulfur compounds e.g. Ajoene** (garlic odor).

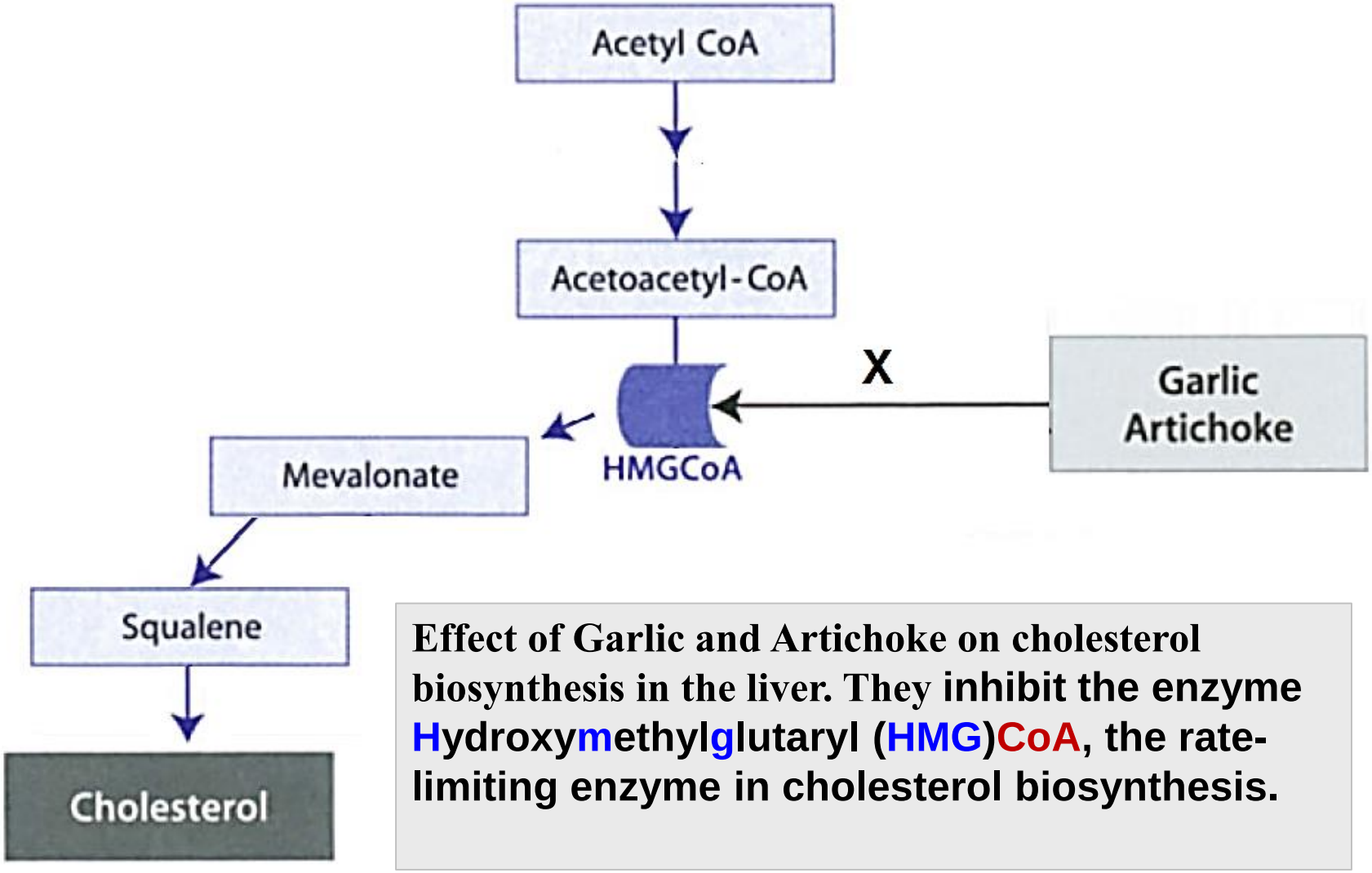
Pharmacological effects of garlic:

a) Treatment and prevention of hyperlypidemia

Allicin is the main pharmacologically active constituent. Garlic act by:

1. **Inhibiting cholesterol biosynthesis**
2. **Enhancing lipase activity → increases triglycerides degradation**
3. **Reduces LDL and increases HDL.**

b) Also, it is used as an adjunct in treatment of hypertension.



Effect of Garlic and Artichoke on cholesterol biosynthesis in the liver. They inhibit the enzyme Hydroxymethylglutaryl (HMG)CoA, the rate-limiting enzyme in cholesterol biosynthesis.

b) Artichoke الخرشوف

- Artichoke **inhibits the oxidation of LDL**
- Its cynarin and flavonoid content **inhibits cholesterol synthesis**

c) Fenugreek بذور الحلبة

- It **increases bile acids excretion** → deplete liver cholesterol.
- Its mucilage content **reduce cholesterol absorption**

d) Psyllium بذور القطونا

The mucilage content:

- It **increases** the **fecal elimination of cholesterol & bile acids**
- It **decreases** the intestinal **re-absorption of bile acids** .

III. Hypertension ارتفاع ضغط الدم

- It is the most common CVD, which occur if blood pressure goes beyond 120/80 (for a young man) and 150/90 mm Hg (for old man).
- Hypertenison is associated with an increased risk of heart failure, renal failure and stroke.
- In about 90 % of cases with sustained hypertension there is no identifiable cause and the term “essential hypertension” is used.
- In about 10% of all cases, hypertension results from other imbalances and so is called "secondary hypertension”.
- Generally treatment of secondary hypertension is the same as for essential hypertension but the cause should be also treated (if possible).

- **Common causes of secondary hypertension include:**
  - **excessive renin release in kidney disease**
  - **hypersecretion of aldosterone and cortisol**
  - **hypersecretion of antidiuretic hormone**

- **Drugs used for treating hypertension include:**
  - **diuretics**
  - **sympatholytics**
  - **direct-acting vasodilators**
  - **calcium channel blockers**
  - **angiotensin converting enzyme (ACE) inhibitors**

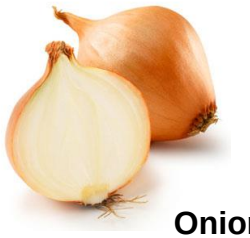
Phytotherapy of hypertension

- **Examples**

Common (Latin) names	Part used	Key comp.	Dose /d
Garlic (*Allium sativum*)*	Bulb	Alliins	4 g
Onion (*Allium cepa*)*	Bulb	Alliins - flavonoids	20 g
Olive (*Olea europaea*)	Leaf	Oleuropein (a complex phenolic glycoside)	6 g
Snake root (*Rauwolfia serpentina*)	Root	Alkaloids (e.g. reserpine)	0.6 g
Roselle (*Hibiscus sabdariffa*)	Caylx	Anthocyanin - flavonoids	

* Supported by German Commission E

Garlic



Onion

Olive Leaves

Snake root

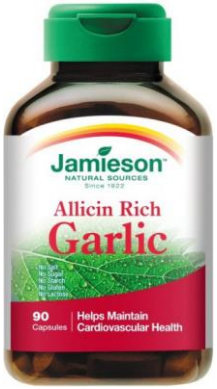
Roselle

a) Garlic (*Allium sativum*) الثوم:

- **Garlic may act by:**
  - **prostaglandins-like hypotensive effect**
  - **inhibiting angiotensin-converting enzyme**
  - **enhancing the synthesis of the vasodilatory NO.**

- **Besides its confirmed antihypertensive effect, garlic also influences other cardiovascular risk factors e.g. thrombosis, diabetes, and high cholesterol through its:**
  - **antioxidant properties**
  - **inhibition of blood aggregation**
  - **reduction of serum cholesterol, triglycerides, and LDL**
  - **enhancing serum HDL**

Dosage forms:



- **Allicin-releasing preparations are most proven in blood pressure management.**

  - ❑ **Garlic capsules (containing garlic powder)**
  - ❑ **Capsules containing garlic oil (contains complex mixtures of organosulfur compounds e.g. diallyldisulfide, diallyltrisulfide and diallyl tetrasulfide).**

- **A daily dose:**
  - **4 g (~ 1 average size clove)**
  - **About 900 mg of dried garlic powder**

How to choose garlic supplements that provide high amounts of Allicin?

- **Garlic powder (dried garlic) preparations:**
  - ✓ They do not contain any **Allicin** but **alliin** and **allinase** .
  - ✓ To preserve the **allinase** activity that is sensitive to **stomach acid**, dried garlic powder is sometimes **enterically coated**, so that some **allicin** can be produced in the intestine.

- **Distilled garlic oil:**
  - ✓ Distilled garlic oil involves **heating** crushed garlic in **boiling water.**
  - ✓ Does not contain **allicin.** **What does contain?**

- **Allicin powder extract:**

✓ Capsule contains 100% stabilized allicin.

✓ Unlike other supplements , it contains a stable amount of bio-available allicin that is ready to be used by the body.

✓ It provides the body with 100% yield of allicin that helps promote your cardiovascular health.

✓ Most effective form of garlic preparations.

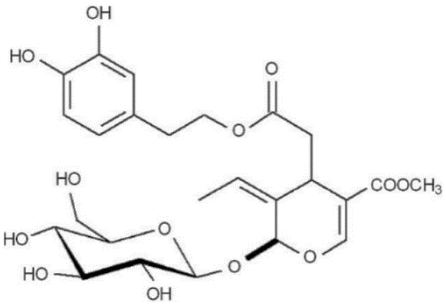
Alliforce™, more effective than other garlic products

Some garlic products can only claim to have the Allicin potential.

This potential is never reached, due to the acidity in the stomach, as has been shown in several clinical studies. In fact, most brands do not even achieve 5% of their claimed yield.

b) Olive leaves (*Olea europaea*) ورق الزيتون :

- It has been proven to lower high blood pressure in clinical trials provided the dose is sufficiently high.



oleuropein

- Olive activity lies in its content of oleuropein exerting:
  - Antioxidant
  - Angiotensin converting enzyme (ACE) inhibition
  - Calcium channel blockage

- Different mechanisms of action create synergistic antihypertensive activity together with low toxicity or side effects.

c) Snake roots (*Rauwolfia serpentine*) جذور الثعبان :

- Snake root is supported by **German Commission E**. Both standardized root preparations and its reserpine alkaloid are officially monographed in the **USP**.

- **Mechanism:** The drug (or reserpine) causes a depletion of noradrenaline from the adrenergic neurons, thus, impairing sympathetic function.

- Due to unacceptable side effects (nightmares and depression), the use of snake root has partially diminished.

d) Roselle (*Hibiscus sabdariffa*) سبلات الكركديه :

The drug was proved to be hypotensive, perhaps through

- **direct vaso-relaxant effect**
- **action on calcium channels**
- **ACE inhibitory effect**
- **diuretic activity**