

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وبینار نقش طب تلفیقی در پیشگیری و کنترل استئوپروز

مرکز تحقیقات استئوپروز، پژوهشگاه علوم غدد و متابولیسم دانشگاه
علوم پزشکی تهران
مهرماه 1400

Osteoporosis and Complementary and Alternative Medicine


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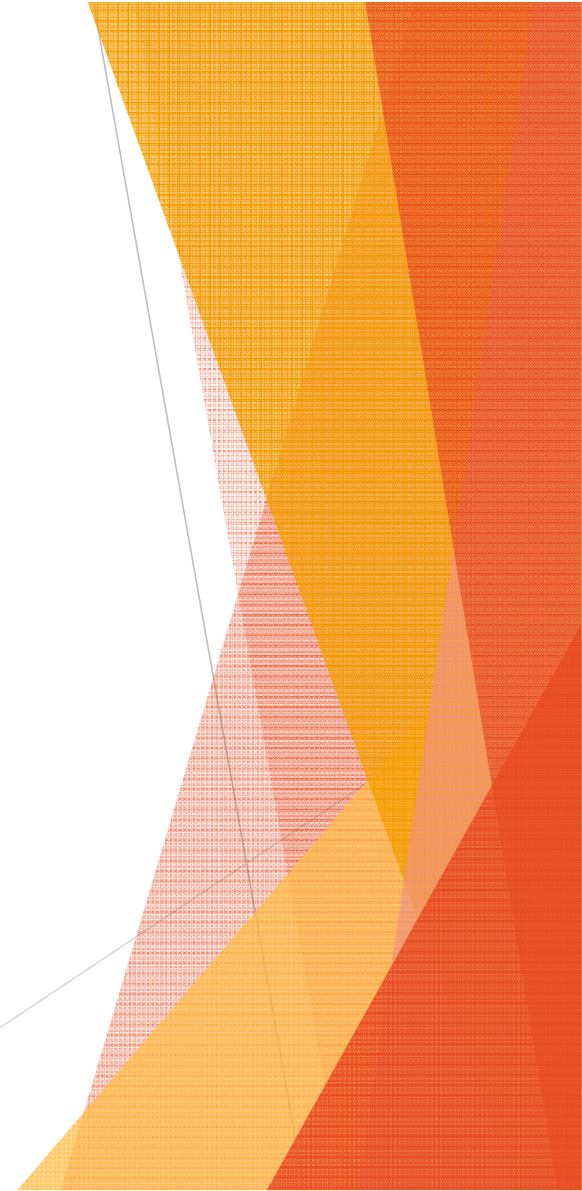
- ▶ Osteoporosis (OP) is a bone disease that is characterized by a decrease in bone density and microstructure quality
- ▶ Clinically, it is defined as a bone mineral density (BMD) 2.5 standard deviations below the mean peak bone mass of the healthy population - known as the T score - as measured by dual x-ray absorptiometry (DXA)

- ▶ The main consequence of osteoporosis is the manifestation of fragility bone fractures due to reduced bone strength and is often seen in the vertebrae, wrists and hip.
- ▶ .



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- ▶ Considering that osteoporosis is a disease of progressive bone loss that affects a large population of elderly people who often require a long term therapy.
 - ▶ it would be of great relevance to search for natural compounds that will provide an alternative and effective way for the treatment of osteoporosis

- ▶ 1) phytoestrogen with estrogenic effects
- ▶ 2) antioxidant and anti-inflammatory agents
- ▶ 3) compounds that exert their effects with pleiotropic actions or unknown mechanisms.



1. PHYTOESTROGENS & TREATMENTS WITH ESTROGENIC EFFECTS

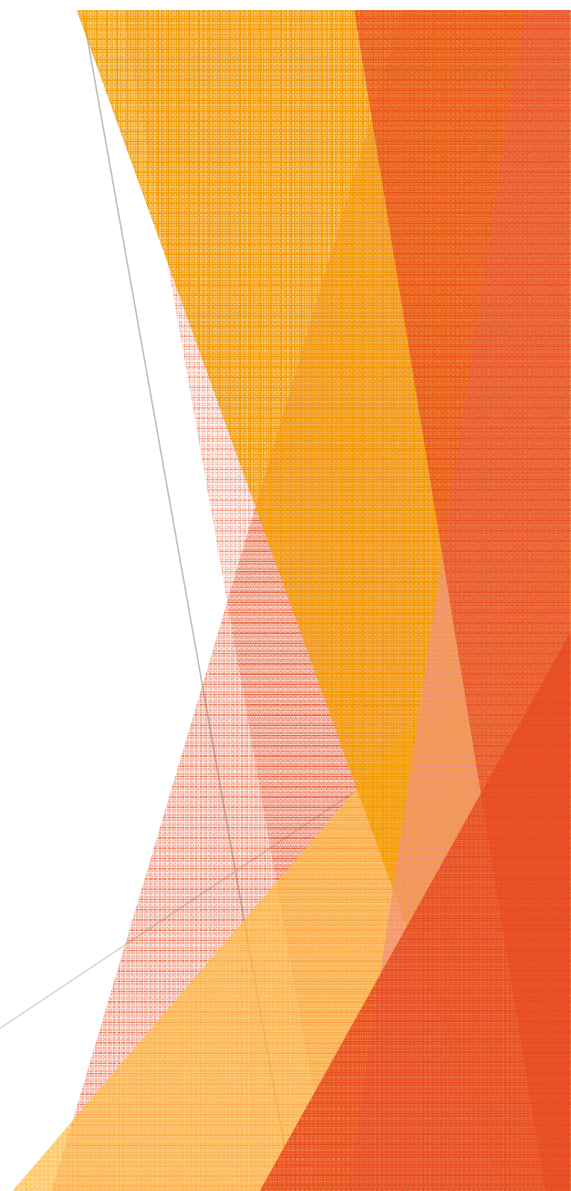
- ▶ Estrogen is involved in the regulation of life cycle and activity of osteoblasts as well as osteoclasts, directly through ER α and ER β , and indirectly through PTH.
- ▶ Estrogen also controls the expression and activity of various inflammatory cytokines involved in bone remodeling.

Genistein, Daidzein,

- ▶ *Erythrina variegata*
- ▶ Soybean
- ▶ *Genista tinctoria*

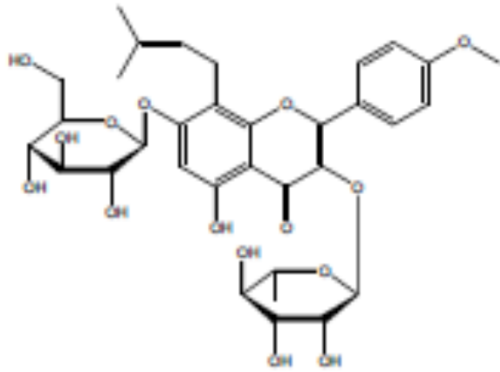


- ▶ Zhang et al. [9] conducted a double blind, placebocontrolled trial in 100 postmenopausal women (85 of 100 completed the trial
- ▶ three phytoestrogens icariin, daidzein, and genistein, supplemented with calcium, against placebo group receiving only calcium.
- ▶

- 
- ▶ Study parameters included BMD, bone turnover, biochemical markers, serum estradiol, and endometrial thickness, and these parameters were measured at baseline and 12 and 24 months.
 - ▶ On trial completion, BMD in women in phytoestrogen group was preserved, especially in the vertebrae but not as much in femoral neck, in comparison to the placebo group.

Icariin

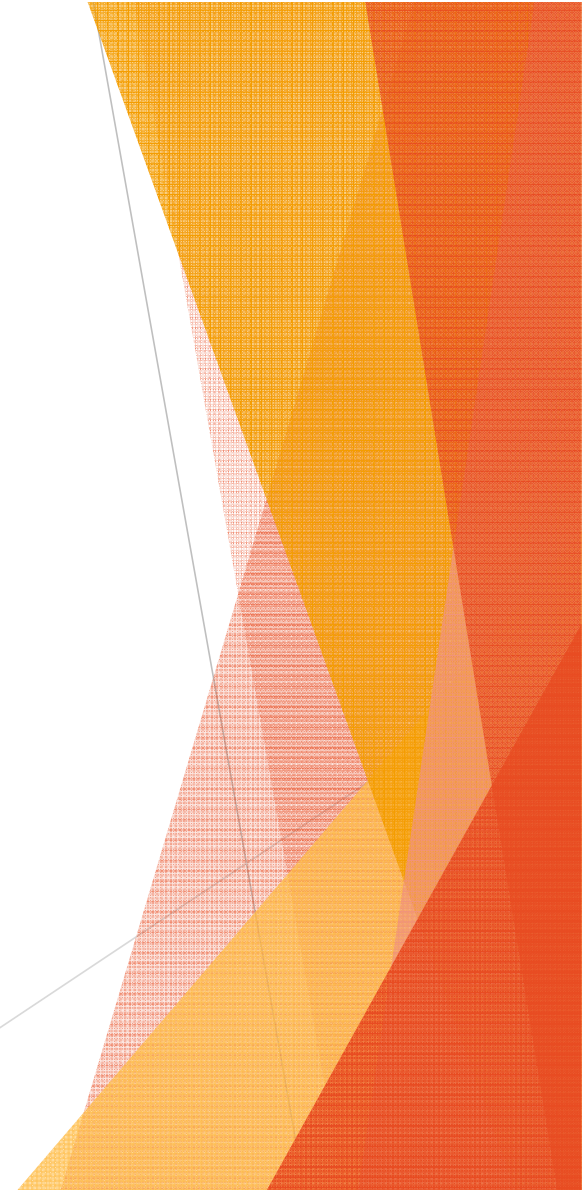
- ▶ Epimedium has been commonly used in traditional Chinese medicine to ‘nourish the kidneys and reinforce the Yang’.
- ▶ According to Traditional Chinese Medicine, kidney system is composed by Kidney Yin and Kidney Yang.
- ▶ Kidney yang is the essential of the yang qi, the latter promotes the functions of the organs and tissues in the whole body.

Icarin		OB, OC	suppress inflammatory osteoclastogenesis; promote osteoblast differentiation through ERK, JNK signal and Wnt/ β -catenin-BMP signaling pathway	mandibular distraction rabbit; OVX rats; OPG-knockout mice	[7, 23] [25-33]
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Berberine

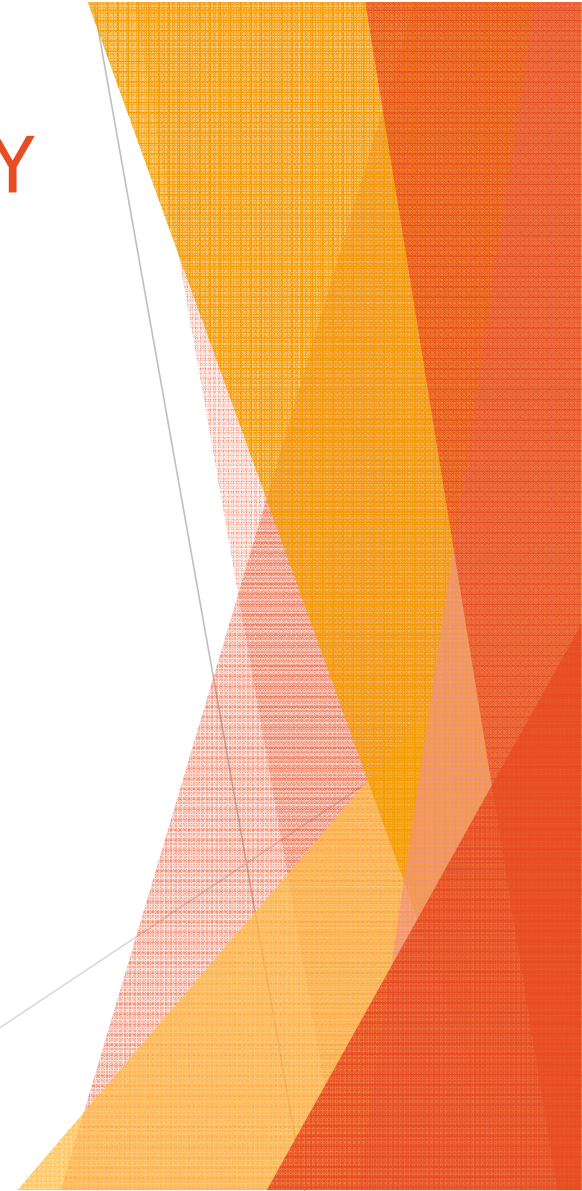
- ▶ Yogesh et al. [44] have explored the effects of *Berberis aristata* extracts, with its proposed active component being berberine, in a rat model. Though not discussed in detail, their discovery of increased rat uterine weight indicates estrogenic properties of *B. aristata* extract.
- ▶ Cold and dry





2. ANTIOXIDANTS & ANTI-INFLAMMATORY AGENTS

- ▶ Green Tea
- ▶ Black Tea
- ▶ Curcumin
- ▶ Feverfew (Parthenolide)
- ▶ Safflower (Carthamus Tinctorius)




Tea

- ▶ Effect of green tea extract on bone turnover markers in type 2 diabetic patients; a double-blind, placebo-controlled clinical trial study

K Mirzaei, A Hossein-Nezhad, M Karimi, MJ Hosseinzadeh-Attar, N Jafari, ...

DARU Journal of Pharmaceutical Sciences, 38-44

- ▶ Green tea shows a strong anti-oxidative stress effect in human primary osteoblasts.
- ▶ It increases the expression of osteocalcin and collagen1A1 in osteoblasts and improves the cell viability.

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- ▶ theaflavin-3,3'-digallate (TFDG), a black tea polyphenol, decreased the formation and differentiation of osteoclasts, suppressed matrix metalloproteinase -2 and -9 (MMP-2 and MMP-9) enzymatic activity and down-regulated MMP-9 expression of osteoclasts.
 - ▶ MMPs are highly expressed in osteoclasts, and play an important role in osteoclast bone resorption. Thus, the authors concluded that TFDG might be a suitable agent for the treatment of osteolytic bone diseases.

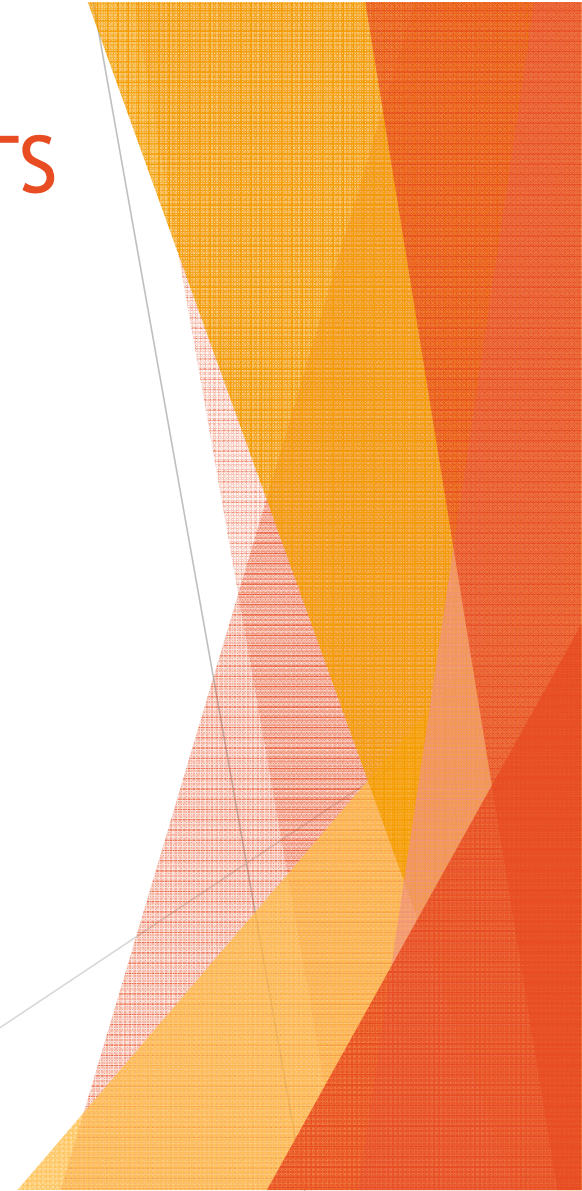
turmeric

- ▶ Curcumin is a component of turmeric and thought to have positive effects on bone. Mice that received curcumin showed an increase in BMD and trabecular bone mass and reduction in the levels of TNF- α and IL-6.



TREATMENTS THAT EXERT THEIR EFFECTS BY MULTIPLE ACTIONS

- ▶ Pomegranate Seed Oil
- ▶ Onion
- ▶ Dried Plum
- ▶ *Cajanus cajan*
- ▶ *Rhizoma drynariae*



pomegranate

Pomegranate	oil extract of seed	punicic acid	suppress expression of CTR, ITG β 3, CA, CTSK MMP 2, MMP9 and TRAP ; anti-inflammation; activate Wnt/ β -catenin pathway.
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Plum

Dried plum


-


dried plum polyphenols








down-regulate NFATc1 and products of inflammation such as NO and TNF- α in osteoclast; upregulate Runx2, Osterix, IGF-I, and RANKL expressions in osteoblast; upregulate BMP-4 and IGF-1 while downregulate NFATc1, P1NP and DPD; antioxidant and modulate immune response



The Value of Plants Used in Traditional Medicine for Drug Discovery

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- ▶ Fossil records date human use of plants as medicines at least to the Middle Paleolithic age some 60,000 years ago.
 - ▶ 1. Solecki R. Shanidar IV, a Neanderthal flower burial in northern Iraq. *Science* 190:880-881 (1975)


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- ▶ However, the value of these systems is much more than a significant anthropologic or archeologic fact.
 - ▶
 - ▶ Their value is as a methodology of medicinal agents, which, according to the World Health Organization (WHO), almost 65% of the world's population have incorporated into their primary modality of health care.

						
Drug	Acetyldigoxin/ digoxin	Adoniside	Atropine	Reserpine	Amiodarone	Verapamil
Plant source	Digitalis lanata Ehrh.	Adonis vernalis L.	Atropa belladonna	Rauwolfia serpentina (L.)	Ammi visnaga	Papaver somniferum L.

The goals of using plants as sources of therapeutic agents


- ▶ a) to isolate bioactive compounds for direct use as drugs, e.g., digoxin, digitoxin, morphine, reserpine, taxol, vinblastine, vincristine.
- ▶ b) to produce bioactive compounds of novel or known structures as lead compounds for semisynthesis to produce patentable entities of higher activity and/or lower toxicity,
e.g., metformin, nabilone, oxycodon, verapamil, and amiodarone

- ▶ c) to use agents as pharmacologic tools, e.g., lysergic acid diethylamide, mescaline, yohimbine
- ▶ d) to use the whole plant or part of it as a herbal remedy, e.g., cranberry, echinacea, feverfew, garlic, ginkgo biloba, St. John's wort, saw palmetto.

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- ▶ The number of higher plant species (angiosperms and gymnosperms) on this planet is estimated at 250,000, with a lower level at 215,000 and an upper level as high as 500,000 .
 - ▶ Only about 6% have been screened for biologic activity, and a reported 15% have been evaluated phytochemically

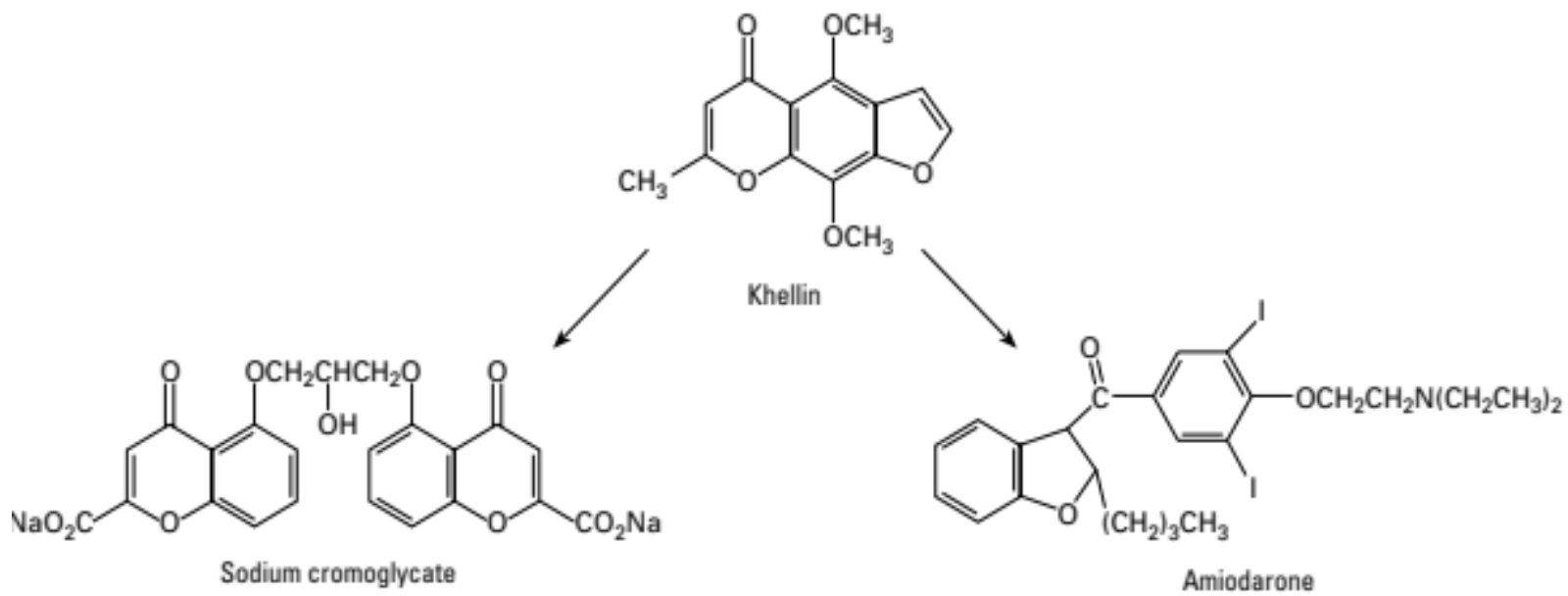
Approaches to Drug Discovery Using Higher Plants

- ▶ Random selection followed by chemical screening.
- ▶ Follow-up of biologic activity reports.
- ▶ Follow-up of ethnomedical (traditional medicine) uses of plants.

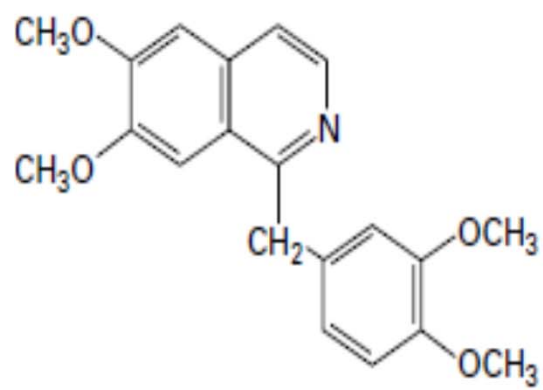
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- ▶ Plants used in organized traditional medical systems.
 - ▶ Ayurveda, Iranian or Persian medicine Unani, Kampo, and traditional Chinese medicine have flourished as systems of medicine in use for thousands of years.

- ▶ Derive name from catalogue of frequently used plants
- ▶ Review literature
- ▶ Evaluate data in literature
- ▶ Decide on need to test
- ▶ Select tests
- ▶ Establish priorities for testing
- ▶ Collect plants
- ▶ Determine type of biological activity
- ▶ Carry out human studies

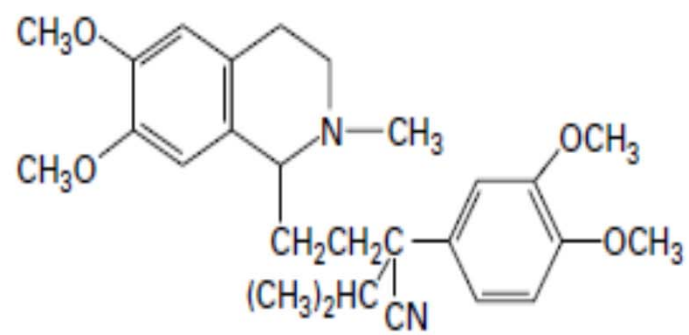




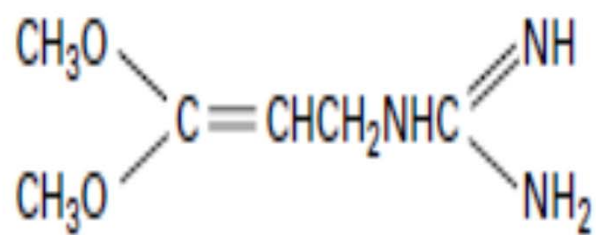
Structural relationship of amiodarone and sodium cromoglycate to khellin.



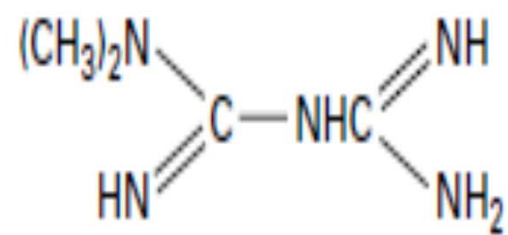
Papaverine



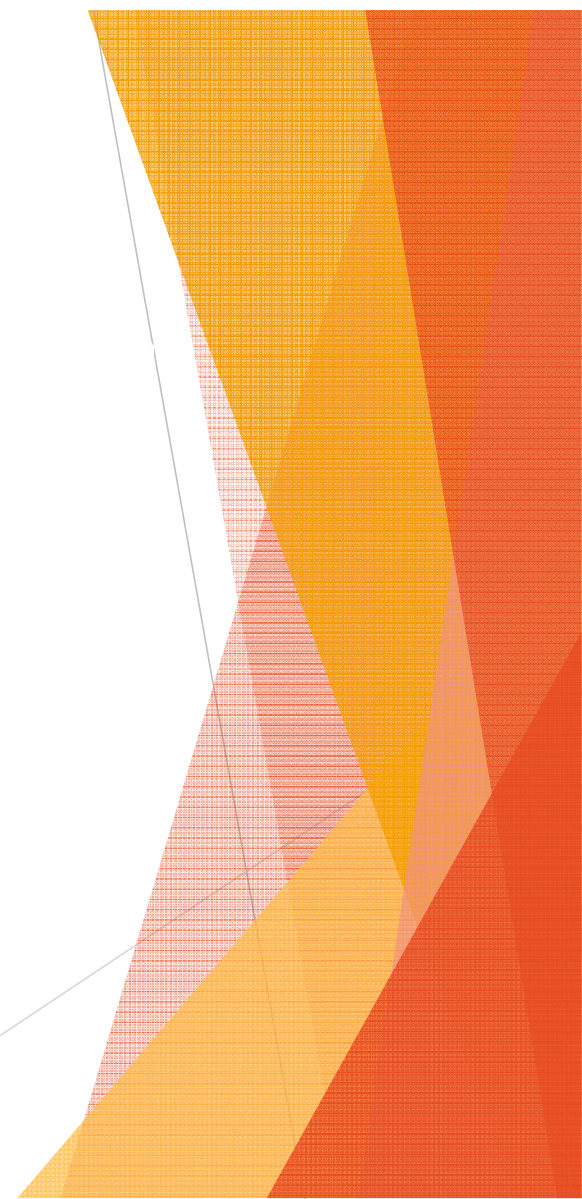
Verapamil



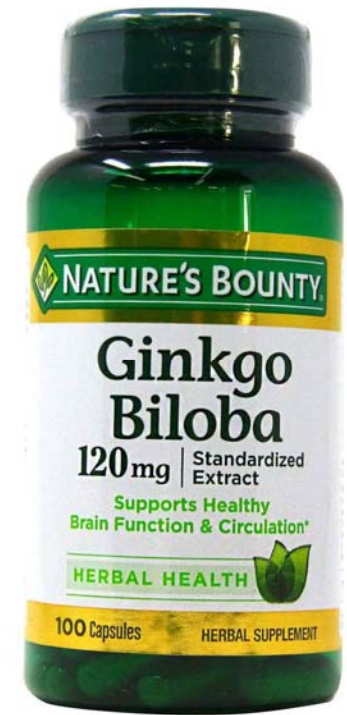
Galegine



Metformin



Ginkgo biloba



Spatholobus suberectus



Butea monosperma



Drynaria fortunei



Green tea



Black tea



Mild ingredients, skin antioxidant function and cost-effective

#Hypoallergenic #AntioxidantAmpoule

NEW Black Tea Youth Enhancing Ampoule

Quick reset solution even for rough and dull skin!
Experience the solid benefits of Black Tea Youth Enhancing Ampoule.



Cudrania tricuspidata s



Eucommia ulmoides



Carthamus tinctorius



Pomegranate



Cissus quadrangularis



Onion



Cimifuga racemosa



Cajanis cajan



Dried plum



Ligustrum lucidum



Rubus coreanus



Astragalus membranaceus



Glechoma hederacea



Coix lachryma-jobi

