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Hıltan tohumunun (*Umbelliferae, Ammi visnaga* L.) düz kaslar üzerine etkisi

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Özet

Hıltan (*Umbelliferae, Ammi visnaga* L.), vücudun kan damarlarını genişletici ve düz kaslardaki spazmları giderici etki gösterir. Bronşiyal yollar ve diğer vücut tüp ve boşlukları: anjin, astım, arteriosikleroz ve böbrek taşı oluşumu için çok elverişlidir. Hıltan tohumlarından hazırlanan tentür, üriner kaslar üzerinde antispazmodik etki göstererek kolayca ağrı kesebilir. Farklı araştırmacıların elde ettiği sonuçlara göre hıltanın düz kaslar da daha etkili olduğu ve kalp kasının kanlanmasını desteklediği görülmüştür. Hıltan, koroner damarları genişletebilir. Kalp ritmini veya kan basıncını artırmaksızın kalbin kapasitesini yükseltebilir.

Anahtar kelimeler: Hıltan tohumu, kellin, visnagin, düz kas.

The effect of khella seed (*Umbelliferae, Ammi visnaga L.*) on smooth muscles

Abstract

Khella (*Umbelliferae, Ammi visnaga* L.) has been used to support the body's efforts to combat spasms in smooth muscles and dilate blood vessels. Bronchial airways and many other bodily tubes and ducts, making it potentially very useful for the management of angina, asthma, arteriosclerosis and kidney stones. A tincture of khella seeds can ease the pain by acting as an antispasmodic on the urinary tract muscles. According to the results obtained by different researchers khella seems to improve blood supply to smooth muscles and makes myocardial metabolism more efficient. It may dilate the coronary vessels, whereby increasing the capacity of the heart without increasing the heart rate or affecting blood pressure.

Keywords: Khella seed, khellin, visnagin, smooth muscle.

1. Introduction

The rationale for the synthetic program was based on the natural product, khellin, which was used in the middle east as a diuretic and antispasmodic. Khellin was isolated from the seeds of the plant *Ammi visnaga*, called in Arabic "khella". The first paper from the Labaz laboratories describes the coronary vasodilator properties of a series of benzofurans derived from the furanochromone structure of khellin (Deltour et al., 1961). Indigenous to the eastern mediterranean region, western Asia and Europe. Cultivated in southern Europe and northern Africa, and in Argentina, Bulgaria, Chile, China, India, Islamic Republic of Iran, Japan, Mexico, Romania, Russian Federation and Turkey (Cox et al., 1951).

The seeds of the herb are the most important part that has medicinal value. Active components of khella, including khellin, come from the fruits and seeds of *Ammi visnaga*. A member of the carrot family (Umbelliferae). The German Commission E Monograph recommends Khella for its ability help the urinary passages heal after the trauma of passing kidney stones by inhibiting irritation and spasms in the urinary canal.

Khella's antispasmodic properties are also useful to treat asthma attacks. During the 1950′s, research into khella's usefulness as an asthma treatment led to the creation of a number of asthma medications. Two chemicals found in khella, khellin and visnagin, ease spasms in the bronchial passages (Harvengt and Desager, 1983).

As early as the 1940′s, studies were done on the effect of khella in treating angina. It soothes angina pain by causing the arteries of the heart to relax and can improve the heart's ability to withstand exercise. Khellin works to increase "good" cholesterol (HDL or high-density lipoprotein) and lower "bad" cholesterol (LDL or low-density lipoprotein), resulting in less plaque formation (Hudsin, 1999).

Khella seems to have some antimicrobial activity. This might be attributable to both the khellin and visnagin constituents, which both seem to have antifungal, antibacterial, and antiviral activity (Vanachayangkul, 2008).

The main constituents are furanocoumarins (2-4%), including khellin (0.3-1.2%), visnagin (0.05-0.3%), khellol, and khellinol and angular pyrano-coumarins (0.2-0.5%), including visnadin, samidin and dihydrosamidin. The tea also contains lipids (up to 18%), furanoacetophenones, flavonoids (flavonol and flavonol sulfates), and 0.2-0.3mL/kg essential oil (Ortel et al., 1988).

2. The Mechanisms of Action

Combining herbs with certain drugs may alter their action or produce unwanted side effects. Don't use khella while taking: blood thinners such as coumadin, heart drugs called calcium channel blockers (such as calan and procardia), other drugs that lower blood pressure. Khella may also serves as mast cell stabilizers.

The major advantage of khellin is that it does not lead to phototoxic skin erythema and thus can be considered safe for home treatment. Because of its photochemistry it may be considered less hazardous than psoralens regarding mutagenicity and carcinogenicity (Wichtl, 1994).

The constituents, visnadin, visnagin, and khellin, all seem to have cardiovascular effects due to calcium channel blocking actions (Fetrow and Avila, 1999). Visnadin is the most active, probably a result of its calcium blocking activity, shown in vitro (Martindale, 1999). It can inhibit vascular smooth muscle contraction and seems to dilate peripheral and coronary vessels and increase coronary circulation (Duarte, 2000). Visnagin also has negative chronotropic and inotropic effects and reduces peripheral vascular resistance (Schindler, 1953). Khellin also acts as a vasodilator and has bronchodilatory activity and spasmolytic activity (Duarte et al., 1997).

In addition, Khella seeds extract showed highly potent diuretic activity. Moreover, the effect of Khella on calcium and oxalate contents in kidneys of rats fed with 3 % glycolic acid was studied. Results revealed the effectiveness of Khella treatment on the inhibition of formation of calcium oxalate in kidney.

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Much of the interest in khellin was directed at its action on the heart, following a serendipitous observation by Gleb von Anrep, the professor of pharmacology at Cairo, who noticed that afterhis laboratory technician had self-medicated his renal colic with it his angina disappeared. Anrep then conducted tests of khellin on the coronary blood flow in dogs, followed by a clinical trial inpatients with angina. This and further studies by Anrep suggested the drug had beneficial effects when given by mouth (Anrep et al., 1948)

Ammi visnaga is an herbaceous plant that grows wild in Egypt; where a decoction from it acquired a reputation in folk medicine as a diuretic that could relieve renal colic. This was a common problem in Egypt arising from renal stone formation associated with schistosomiasis. A study on a refined extract by K. Samaan at the University of Cairo in1930 revealed its ability to relax smooth muscle, including that of the ureter and coronary arteries, in a variety of animal species (Quart, 1930).

A subsequent placebo-controlled study of 36 people found that a topical khellin gel plus UVA caused epigmentation in 86.1% of the treated cases, as opposed to 66.6% in the placebo group (Orecchia et al., 1998).

A potent vasodilator of coronary and bronchial passages. Effects relaxation of all smooth muscles by direct action. Outstanding because small doses produce pronounced and prolonged arterial dilation without hypotensive complication thus permitting administration when abnormal blood pressure complicates the anginal syndrome. Khellin is most rapidly absorbed from the small intestine; gastric absorption is slow (Barsoum, 1947).

A double-blind, placebo-controlled study of 60 people indicated that the combination of oral khellin (which is the main constituent of *Ammi visnaga*) and natural sun exposure caused repigmentation in 76.6% of the treatment group; in comparison, no improvement was seen in the control group receiving sunlight plus placebo (Abdel-Fattah et al., 1982).

3. Conclusion

Ceramic typical doses of khella tincture are 1–3 mL, three times per day, or more often, as needed. Typical doses of henbane 1:5 tincture are 3–5 drops, three times per day, or as needed until a slight dry mouth or dry eyes develop (Yarnell and Abascal, 2011). Infuse 1 table spoon of crushed seeds per cup of water and drink twice a day or take 20 mg standardized to 12% of the active constituent khellin a day. Khella should not be taken with the medication digoxin.

Subsequent studies were generally in favour of the use of khellin for angina as it had a longer duration of action than had glyceryl trinitrate.

Khellin and visnagin have spasmolytic activity that could relax the smooth muscle which might extend the urological tube and help remove stones easily from the urological system (Schindler, 1953; Gunaydin and Beyazit, 2004). This can inhibit vascular smooth muscle contraction, dilate peripheral and coronary vessels and increase coronary circulation.

The amiodarone research program seeking an improved anti anginal agent was based on the unsubstantiated efficacy of khellin in angina pectoris (Rosenbaum, 1974).

Pure khellin (dimethyoxymethyl-furanochromone) is the active principle of *Ammi visnaga* unadulterated by visnagin and other constituents which tend to produce undesirable side effects. It is presented in enteric-coated tablets for selective action (Bagouri, 1949).

Khellin exerts no stimulating effect on the sympathetic nervous system. It is, therefore, unlikely that its coronary vasodilator action is similar in nature to that produced by adrenaline.

As with other smooth muscles it acts directly on the muscle fibres of the blood vessels. The apparently selective action of khellin on the coronary blood vessels is due to their much greater sensitivity to the drug as compared with the systemic blood vessels.

This preliminary clinical trial, following physiological experiments, seems sufficiently favourable to justify a further and more extensive therapeutic test of khellin in angina pectoris and coronary occlusion. Khellin, the active principle of *Ammi visnaga*, has been tested physiologically in dogs, both on the heart-lung preparation and on the whole animal, in regard to its effect on the heart and coronary circulation. It was found to be an effective vasodilator with a selective action on the coronary vessels, so that coronary flow was increased by doses insufficient to lower the general blood pressure.

6. Kaynaklar

1. Deltour, G., Binon, F., Henaux, F., Charlier, R. Recherches dans la série des benzofuranes. I–Benzofuranes possédant une activité coronarodilatrice [Research into the benzofuran series. I. Benzofuranes with coronary dilator activity]. Arch Int Pharmacodyn. 131:84-106, 1961.
2. Cox, J.S.G. et al., Disodium cromoglycate. Adv Drug Res; 5:115, 1970.
3. Harvengt, C. and Desager, J. P. Hdl-Cholesterol Increase in Normolipemic Subjects on Khellin - A Pilot-Study, International Journal of Clinical Pharmacology Research. 3:363-366, 1983.
4. Hudsin, T. G. J. Phytomedicines as antivirals, Drugs Fut., 1999.
5. Vanachayangkul, P. Ammi visnaga L. For The Prevention Of Urolithiasıs. A Dissertation Presented To The Graduate School Of The University Of Florida In Partial Fulfillment Of The Requirements For The Degree Of Doctor Of Philosophyuniversıty Of Florida, 2008.
6. Ortel, B., Tanew, A., Honigsmann, H. Treatment of vitiligo with khellin and ultraviolet A [see comments]. J Am Acad Dermatol. 18(4 Pt 1):693-701, 1988.
7. Wichtl, MW. Herbal Drugs and Phytopharmaceuticals, Medpharm GmbH Scientific Publishers, Bisset. Stuttgart, 1994.
8. Fetrow, C.W. and Avila, J.R. Professional's Handbook of Complementary & Alternative Medicines, Springhouse, PA., 1999.
9. Martindale, M. Martindale the Extra Pharmacopoeia, Pharmaceutical Press, 1999.
10. Duarte, J., Torres, A. I. and Zarzuelo A. Cardiovascular effects of visnagin on rats, Planta Medica. 66:35-39, 2000.
11. Schindler, H. The genuine ammei, Ammi visnaga (L.) LAM, a Mediterranean spasmolytic drug with khellin content., Pharmazie. 8:176-179, 1953.
12. Duarte, J., Vallejo, I., Perez Vizcaino, F., Jimenez R., Zarzuelo A. and Tamargo J. Effects of visnadine on rat isolated vascular smooth muscles, Planta Medica. 63:233-236, 1997.
13. Yarnell, E. and Abascal, K. Spasmolytic Botanicals. Relaxing Smooth Muscle with Herbs. Vol. 17, No: 3, 2011.
14. Anrep, G., Kenaway, M.R., Barsoum, G.S. Coronary vasodilator action of khellin. Am. Heart J., 1948; 37: 531–42.
15. Quart. S.K. J. Pharm. Pharmacol., 1930; 4: 25.

16. Orecchia, G., Sangalli, ME., Gazzaniga, A., et al. Topical photochemotherapy of vitiligo with a new khellin formulation: preliminary clinical results. J Dermatol Treat. 1998;9:65–69.
17. Barsoum, G. S., Kenawy, M. R. and El-Sheehy, A. (1947):J. Roy. Egypt. Med. Assoc., 30, 312.
18. Abdel-Fattah, A., Aboul-Enein, MN., Wassel, GM., et al. An approach to the treatment of vitiligo by khellin. Dermatologicia. 1982;165:136–140.
19. Gunaydin, K. and Beyazit, N. The chemical investigations on the ripe fruits of Ammi visnaga (LAM.) Lamarck growing in Turkey, Natural Product Research. 18:169-175, 2004.
20. Rosenbaum, M.B., Chiale, P.A., Ryba, D., Elizari, M.V. Control of tachyarrhythmias associatedwith Wolff–Parkinson–White syndrome by amiodarone hydrochloride. Am. J. Cardiol., 1974; 34: 215–23.
21. Bagouri, M. M. J. Pharm. Pharmacol., I , 1949. 177.