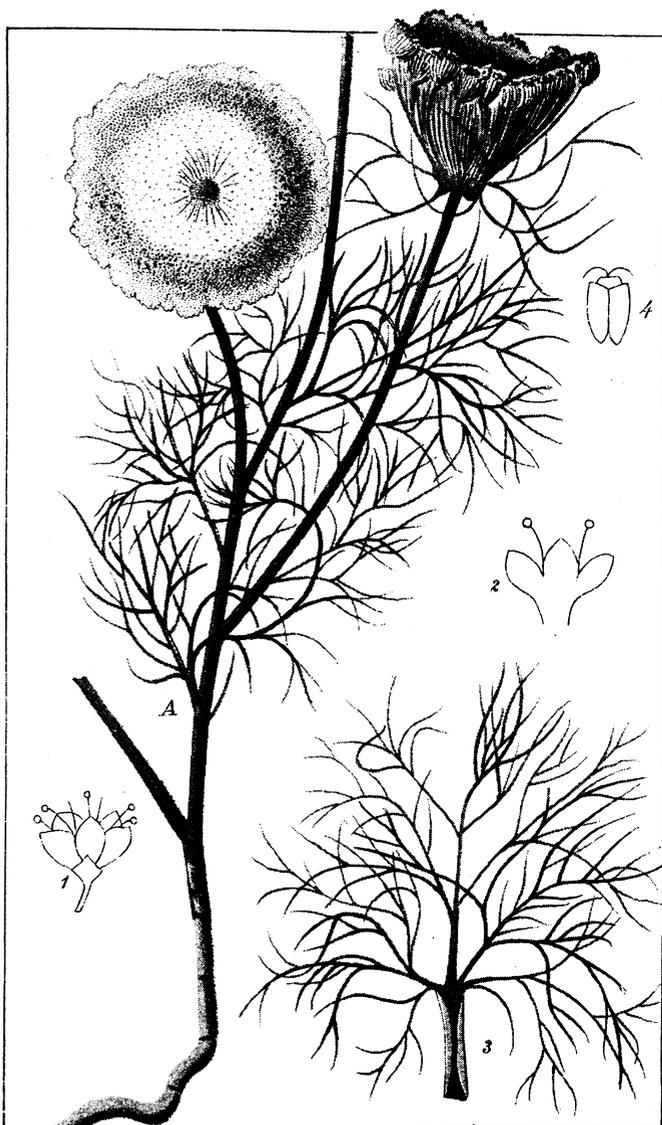


PLANTS IN CARDIOLOGY



Royal Botanic Gardens Kew.

C. Bettfreund et al. descrip. *Fl. Conans. Kapp. pino.* 9. Guernsester. 1814155. *Ammi visnaga* L.*Ammi visnaga* (L.) Lam. Bettfreund C. *Flora Argentina*. 1901: plate 155.

Amiodarone, nifedipine, sodium cromoglycate

Ammi visnaga is a herbaceous Mediterranean plant belonging to the family Umbelliferae, named after *umbra* a shadow or shade. The binomial name is from antiquity and has no special meaning while in Egypt the plant is called khella. When dried the stout flower stalks were used as toothpicks hence the early French name, "herbe aux curedents".

People living on the Nile delta often had renal stones because urinary schistosomiasis was common. For many centuries khella, which is common in the delta, was known to relieve renal colic. The seeds (fruits) contain the active principle khellin—first extracted in

1879 and identified at Cairo University in 1932 as a chromone. Khellin works by relaxing the smooth muscle of the ureter.

It was, however, a chance observation in 1945 by G V Anrep, a pupil of both Pavlov and Starling, that led to the development from khellin of modern drugs for asthma and heart disease. Anrep was Professor of Pharmacology in Cairo and his technician who had severe angina got renal colic and treated himself with khella. When the man returned to work Anrep perceptively noticed that he no longer had angina and this stimulated him to investigate the effect of khellin on the heart. Using the heart-lung preparation Anrep measured the coronary blood flow in dogs and showed that khellin was an effective and selective coronary vasodilator. Then he did a clinical trial in patients with angina which gave favourable results. His seminal paper reporting these findings was published in the *British Heart Journal* (1946;8:171-7.)

This stimulated research elsewhere; and in Belgium the work of R Charlier and J Broekhuysen, who prepared hundreds of compounds with emphasis on the benzofurane portion of khellin, led in 1961 to the synthesis of amiodarone. The name is derived from *am*, to indicate the presence of an amine function; *iod*, for the iodine moiety; and *arone* from benziodarone, an earlier drug in the ketonic benzofurane group.

F Bossert, working for the Bayer company, decided to use khellin as the starting point for his endeavour to find a coronary vasodilator that worked intravenously as well as orally. After 16 years' work he found a promising dihydropyridine compound and two years and 2000 derivatives later he and Vater produced nifedipine. In Britain Anrep's work catalysed research for a new bronchodilator and sodium cromoglycate, Intal, resulted from the work of an asthmatic doctor, Roger Altounyan, who did all the experiments on himself. Paradoxically its unique mode of action is to prevent the release of mediators of bronchoconstriction and not by bronchodilatation.

Several species of Umbelliferae contain fumocoumarins that are photosensitisers and greatly enhance the action on the skin of ultraviolet radiation. An important one is present in *Ammi majus* L. called ami by Galen and known in Egypt as *regl el ghorab*. It is a psoralen called methoxsalen and when given orally with long wavelength (ultraviolet A) radiation it constitutes PUVA therapy. This has achieved considerable success in treating psoriasis (long known to improve with sunlight) and also vitiligo, and is useful in mycosis fungoides. Some umbellifers such as *Pastinaca sativa* (wild parsnip) are notorious for producing severe contact dermatitis in sunlight, which reminds one of the photosensitivity of amiodarone. As a genus *Ammi* must be unsurpassed as a source of important medicines.

A HOLLMAN