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From Tonic to Psoriasis: Stalking Celery's Secrets

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Historical Uses for Celery

Celery has figured as a natural medicine in different cultures throughout recorded history. And since the mid-twentieth century, scientists have been testing the allergenic components of celery and related vegetables. Most Americans think of celery as nothing more than a relatively harmless vegetable. It is also used primarily by vegetarians as a source of fiber and naturally occurring vitamins. But present scientific interest, combined with knowledge gained in the laboratory, may demonstrate that we take such plant foods for granted.

When I was growing up in the Bronx, New York, I didn't think there was anything unusual about drinking celery tonic. My family and friends drank it all the time. Most neighborhood delicatessens in New York sold Dr. Brown's Cel-Ray to accompany and stimulate the pleasures of corned beef or pastrami on rye.

Celery tonic is in fact a euphemism for celery-flavored soda. It tastes like what it is: carbonated water mixed with the juice of crushed celery seeds. Dr. Brown's Cel-Ray is probably the only vegetable-based, bottled soft drink sold in the US, if not in the entire world. That distinction doesn't appeal to everybody, however. Harry Gold, marketing director for Cel-Ray—now manufactured by Canada Dry in Flushing, New York—told us that it's sold throughout the US, but with limited distributions in each state. Devotees return to the same stores year after year, creating a small but geographically stable consumer market.[1]

When the drink first appeared in Brooklyn, New York, in 1869, it was called "Dr. Brown's Celery Tonic."[1] We could not determine whether a real Dr. Brown actually invented the drink, or whether the name was simply adopted as an advertising gimmick. However, it was quite common in those days for all kinds of "tonics" to be advertised. Indeed, the word "tonic" was dropped from the label about 60 years ago at the insistence of the federal government.[1] The public evidently confused Celery Tonic with elixir of celery, whose reputation as a treatment for nervous afflictions has persisted throughout this century. Nevertheless, aficionados like me will continue to call it celery tonic no matter what the Food and Drug Administration (FDA) says.

The Dispensatory of the United States of America was originally written by Philadelphia physicians G.B. Wood and F. Bache. Its nineteenth (1907) edition was rewritten by H.C. Wood, University of Pennsylvania, Philadelphia, and other Pennsylvania physicians. That edition included a recipe for "Compound Elixir of Celery." In addition to the supposedly calming properties of celery, the elixir

combined two powerful depressants—alcohol and coca—with cola, a source of caffeine still used recklessly in many soft drinks.[2] The first edition of *Potter's New Cyclopaedia of Botanical Drugs and Preparations* also appeared in 1907. In it, herbalist R.C. Wren recommends not only the elixir, but the pure seed extract, as a "carminative [or anti-flatulent], diuretic, tonic, and aphrodisiac!"[3] An herbalist is someone who collects and deals with herbs, particularly medicinal herbs. Despite such attractions, Horatio C. Wood, Jr., Philadelphia College of Pharmacy and Science, who had assisted in compiling the 1907 *Dispensatory*, denied in 1928 that celery seed possessed any tonic properties.[4]

Nonetheless, *Henley's Twentieth Century Book of Formulas, Processes, and Trade Secrets*, edited by G.D. Hiscox (1822-1908), contains a recipe for "Celery Compound." This brew adds hyoscyamus—an alkaloid, or organic basic substance usually found in plants, whose toxic effects resemble those of belladonna—to the earlier combination of celery extract, alcohol, and coca.[5] And, as recently as 1983, the FDA recalled a mixture sold as "Iron Kola and Celery Compound," manufactured in Tennessee, whose label failed to list isopropyl alcohol as part of the formula.[6]

The monumental treatise *Pharmacopoeia Universalis*, written by English physician Robert James (1705-1776) in 1747, reveals that during the eighteenth century, celery was far better known as a medicinal herb than as a garden vegetable. James recommends it as a diuretic, a digestive aid, and an anti-lactogen for nursing mothers.[7] (p. 234-5) An anti-lactogen is any substance that suppresses lactation, or the secretion of milk. James also mentions that celery seed distillate was popular as an aphrodisiac.[7] (p. 283) In her tantalizing 1926 history *The Magic of Herbs*, herbalist Mrs. C.F. Leyel tells us that Madame de Pompadour, mistress of Louis XV of France, fed the king celery soup with the same purpose in mind.[8]

Celery originated in the salty marshlands of Europe and northern Asia. *Apium graveolens dulce*, the official Latin botanical name, belongs to the family Umbelliferae. According to M. Ashraf and M.K. Bhatty, Pakistan Council of Scientific and Industrial Research, Karachi, that group includes not only parsley and carrots, but hemlock, the legendary shrub whose poisonous juice killed Socrates.[9] In Europe, "celery" can also refer to celeriac, a related root vegetable classified as *Apium graveolens rapaceum*.

W.A. Warid, professor of agriculture, University of Libya, Tripoli, tells us in the *Encyclopaedia Britannica* that the French were growing both celery and celeriac, mainly for soups and stews, by the 1620s.[10] (p. 43) Cultivation of celery certainly was long-established by 400 BC. According to James, Hippocrates noticed that smallage (wild celery) produced a stronger diuretic effect than celery grown in gardens.[7] (p. 234) In fact, growing celery for medicinal purposes may date back as far as ancient Egypt.[10] (p. 43) And, as we will see, many years of cultivation have turned celery into a worldwide industry.

Celery and Modern Industry

Celery farmers must meet the exacting demands of a vegetable known to its growers as a "prima donna." Celery is particularly sensitive in the first weeks of its life; therefore, most commercial growers plant their seeds in indoor "flats," which are boxes designed for starting seeds inside, rather than in outdoor seedbeds. Kim W. Foreman, a writer for *Organic Gardening and Farming*, claims that celery does not grow

well in temperatures below 50° F or above 80° F.[11] When seedlings appear, usually two to three weeks after sowing, they need another seven to eight weeks in a controlled greenhouse environment before they can be safely transferred outside.

Having originated in swampland, celery prefers a boggy, acidic soil with a high nitrogen concentration—the type of medium that growers call "muck," according to Mark Russell, staff reporter, *Wall Street Journal*.[12] Foreman and Nancy Pierson Farris, another writer for *Organic Gardening and Farming*, suggest that celery needs a growing season of about 100 cool days—that is, a period during which temperatures remain below 80° F.[11,13] Actual growing time varies according to climate, soil, and hybrid type. Midwestern US growers usually set out their seedlings in late summer to let them mature in the fall. Growers in warmer climates take advantage of their frost-free winters, waiting until fall before they set their plants outside.

Michael Rogers, general editor, *Newsweek*, reported a successful experiment with celery by Keith Redenbaugh, Plant Genetics, Inc., Davis, California. The company had used plant-tissue culture techniques to grow "synthetic" celery seeds from cultured stem tissue.[14] The seeds are actually plant somatic embryos. They are genetically complete but lack the normal protective seed coating of celery seeds. Thus, Redenbaugh also had to develop an organic jelly (sodium alginate, a natural seaweed extract) to protect the embryos until they could "fend for themselves."[15] But these synthetic seeds offer some definite advantages for celery growers. The seeds are clonal copies of one another, so they provide uniformity in growing and harvesting selected, elite parent plants. Such enterprising research has a long way to go, however, before it can affect mass production.

Celery is an important cash crop in the US—especially now that Americans are recognizing the dietary importance of fiber and fresh vegetables. A 1961 study of celery harvesters headed by Donald J. Birmingham, US Public Health Service, Cincinnati, Ohio, tells us that celery was imported to Michigan from Scotland in 1856.[16] Today, Michigan remains one of the three major celery-producing states. (California and Florida are the other two.) The US Department of Agriculture (USDA) reports that in 1983, the national harvest from 35,000 acres exceeded 879,000 tons. While less than 10 percent is exported (73 tons), it is valued at over $234 million.[17]

Every year, the celery industry creates thousands of jobs for crop workers both here and abroad. But harvesters and other processors risk a severe allergic reaction, especially if handling a crop infected with fungus, or wet plants. The wet plants transmit the substance capable of causing an allergic reaction more readily than dry ones. We recently discussed allergies in *Current Contents®*.[18] The first recorded case of celery allergy afflicted a French harvester in 1926, according to S.A. Henry, a British health inspector writing in the 1930s.[19,20] Since then, medical literature has described reactions ranging from virulent outbreaks of dermatitis among cannery workers[19,20] and harvesters,[16] to anaphylactic shock brought on by celery consumption, alone or aggravated by exercise.

In 1983, James M. Kidd II and colleagues, Medical College of Wisconsin and Marcus Center for Immunologic and Allergy Research, Milwaukee, Wisconsin, published case reports on four patients who exercised either shortly before or shortly after eating celery.

All reported allergic symptoms that included hives, itching, weakness, and dizziness.[21]

The industrial outbreaks represent two kinds of dermatitis. One, discussed in 1979 by M. Forsbeck and A.-M. Ros, Department of Dermatology, Sodersjukhuset, Stockholm, Sweden, is caused by skin contact independent of other stimuli.[22] The other, which Birmingham's group studied 25 years ago, occurs when skin contact is followed by exposure to light.[16] Both types of exposure produce the same symptoms: itching and burning in the contact area—usually the hands and forearms—followed by a swollen, blistering red rash, the severity of which varies according to individual susceptibility. Symptoms can last from a few days to more than two months, although prolonged duration is very rare.

It is hard to tell whether photoexposure might have worsened the reaction in uncontrolled conditions, for example, in Henry's retrospective studies of British cannery workers.[19,20] However, patch tests have isolated the aromatic celery oil, usually called apiol, as a potent allergen, or substance capable of causing an allergic reaction in itself. Although most highly concentrated in the seeds, apiol is found in all parts of the celery plant. Its main active ingredient is limonene, a terpene, or cyclohexane hydrocarbon, also found in citrus plants (see Figure 1). One of the cannery workers mentioned in Henry's 1938 study had suffered a comparable skin reaction when peeling citrus fruits.[20] D.L.J. Opdyke, Research Institute for Fragrance Materials, Englewood Cliffs, New Jersey, states that limonene is also found in certain types of mint.[23]

Birmingham's group observed and documented a fierce outbreak of dermatitis among Michigan harvesters early in 1959. Among the least susceptible were shed and greenhouse workers, who

Figure 1: The terpene limonene.

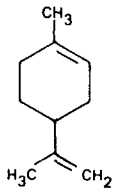
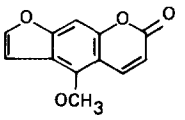
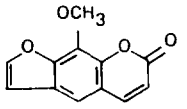


Figure 2: Two furocoumarins, bergapten (A) and xanthotoxin (B), found in healthy celery plants.



(A)



(B)

avoided both photoexposure and contact with a wet crop.[16] The Michigan workers themselves attributed their symptoms to "pink-rot," a common name for the fungus *Sclerotinia sclerotiorum* that infects celery plants.[16] Indeed, the worker's skin tests showed no reaction to healthy celery. Perhaps the harvesters had developed immunity to the allergen levels in a normal crop.

In 1983, dermatologists Joar Austad and Gunnar Kavli, University of Oslo, Norway, published the results of a 1981 study that agree with the findings of Birmingham's group for both infected and uninfected plants.[24] However, the studies by Forsbeck and Kidd corroborate the earlier findings of researchers Joseph F. Palumbo and E.V. Lynn, Massachusetts College of Pharmacy, Boston.[25] All three studies agree that overexposure to healthy celery can cause severe anaphylaxis, aggravated by the pink-rot fungus. The chief chemical agents involved are bergapten and xanthotoxin—furocoumarins (crystalline lactones) found at low levels in normal celery, and at much higher levels in the presence of *Sclerotinia*. Figure 2 shows the chemical

structures of these two furocoumarins found in healthy celery.

Interestingly, a search of ISI®'s 1983 and 1984 files shows that only five research fronts, out of the 10,000 we identified, involve celery directly. Three others concern the connection of photosensitivity with furocoumarins and related substances. (Table 1 lists all eight of these fronts.) One front, #83-5023, includes among its citing authors Kavli, who published a series of papers on furocoumarins of *Heracleum Laciniatum*.[26-30] Kavli coauthored the paper with Austad mentioned above.[24] I will discuss the research fronts in more detail later in this essay.

Celery as Medicine Today

Chemical analysis of celery confirms that it is a wholesome vegetable despite its potential hazards. It provides iron, calcium, sodium, potassium, phosphorous, and traces of other minerals, as well as vitamins A, B, and C. However, plant breeders concerned with "packaging" have eliminated most of the plant's carotene, its source of vitamin A, in creating paler and more mild-tasting hybrids.

While the 1969 handbook *Common and Uncommon Uses of Herbs for Healthful Living* by herbalist Richard Lucas merely recommends celery for rheumatism, arthritis, and "nervousness,"[31] herbalist Juliette de Bairacli Levy, author of *Herbal Handbook for Everyone*, prescribes celery for every ailment from rheumatism and sciatica to liver disorders, hypertension, and even poor eyesight.[32] On a less extravagant note, the 1977 edition of *Martindale: The Extra Pharmacopoeia*, edited by Ainley Wade, Pharmaceutical Society of Great Britain, included a British standard specification for celery oil, followed by the comment that the oil "has been used" as an antispasmodic and a rheumatism remedy.[33]

Such assertions would pass unchallenged in the Orient, where celery is used almost exclusively as a medicine. A 1966 translation of the medieval *Medical Formulary or Aqrābādhin of Al-Kindī* by M. Levey, University of Wisconsin, Madison, includes commentary on present-day Oriental medical practices, many of which can be traced to ancient sources. Iranians boil the aromatic seed oil and inhale the vapor as a cure for headaches.[34] (p. 324) In Egypt, wild celery seed is used as a diuretic, digestive aid, and emmenagogue, a substance that induces menstruation in non-pregnant women.[34] (p. 325) In his 1958 study *Indigenous Drugs of India*, reprinted in 1982, Col. Sir R.N. Chopra, former di-

Table 1: *SCI®/SSCI®* research fronts related to celery. A = number. B = name. C = number of core papers. D = number of citing papers. The year of the front is designated by the prefix in column A.

A	B	C	D
	1983		
83-2593	Soil salinity, irrigation and fertilizer effects on crop yield of celery	2	29
83-4535	8-methoxypsoralen and furocoumarins for psoriasis and PUVA therapy	19	171
83-5023	Isolation, phototoxicity and resulting psoriasis from furocoumarin psoralens	5	37
83-7245	Effect of solutions on seed germination of plants including celery	2	9
83-9097	Effect of seedling emergence time, soil composition and other factors on the maturity and yield of carrots and other vegetable seeds	2	9
	1984		
84-1465	Effects of soil and water salinity on growth and yield of wheat, tomato and other crops	5	40
84-2710	Dithranol, 8-methoxypsoralen and other psoralens in the treatment of psoriasis	23	193
84-7205	Primary effects of ethanol and other agents on seed germination	5	35

rector, Drug Research Laboratory, School of Tropical Medicine, Calcutta, not only lists celery as an emmenagogue, but also condemns attempts to use it as an illegal abortifacient,[35] (p. 495; 563-7) that is, as a drug used to induce abortion.

S.P. Mital and colleagues, New Delhi Indian Agricultural Research Institute, mention that most of the celery grown for seed, rather than as a vegetable, is grown in India.[36] The seeds are exported to other countries where they are used to manufacture such products as culinary sauces, oleoproteins, and nerve tonics. Therefore, that country has taken important steps to combine eastern tradition with western laboratory technology. In 1971, A. Kar and S.R. Jain, Department of Pharmaceutical Sciences, University of Saugar, India, published results presumably confirming the antibacterial effect of celery and other aromatic plants.[37] Jain cited that study in an article on natural fungicides, coauthored with M.R. Jain and published in *Planta Medica* in 1973.[38] A 1980 report by S.K. Garg and colleagues, Department of Chemistry, University of Delhi, describing their own work with glucosides occurring in celery, also appeared in that journal.[39]

Research Fronts Involving Celery

As mentioned earlier, there are five research fronts specifically related to celery in Table 1. Much more research (#83-4535, #83-5023, and #84-2710) concerns the mechanism of photosensitivity of 8-methoxypsoralen and furocoumarins for psoralens and PUVA therapy. Psoralens are substances found in some plants that, when administered to patients, increase the skin's sensitivity to light. As described by dermatologist Dorothy I. Vollum, Lewisham Hospital, London, PUVA therapy is a type of photochemotherapy that combines psoralen and long-wave ultraviolet (UVA) irradiation and is used to treat psoriasis, a chronic inflammatory skin disease.[40] Of the 19 core papers in #83-4535, the paper most cited is "Risk of cutaneous carcinoma in patients treated with oral Methoxsalen photochemotherapy for psoriasis" by dermatologist R.S. Stern and colleagues, Beth Israel Hospital, Massachusetts General Hospital, and Harvard University, School of Public Health, Boston, Massachusetts.[41] This paper is cited by 57 of the 171 papers published in 1983 on this topic. This 1979 paper has attracted a lot of attention—267 citations since it appeared, and 23 in 1984 alone. Psoralen therapy continued to be an active area of research in 1984, as is shown by research front #84-2710. The core paper most cited in this front is by P.S. Song, Department of Chemistry, Texas Technical University, Lubbock.[42] Published in 1979, this paper was cited by 39 of 193 papers from 1984 on this topic.

Research front #83-5023, "Isolation, phototoxicity, and psoriasis from furocoumarin psoralens," was identified by five core papers, the most-cited being "Phototesting and dosimetry for photochemotherapy" by K. Wolff and colleagues, Department of Dermatology, University of Vienna.[43] Published in 1977 in the *British Journal of Dermatology*, this paper was mentioned in 14 of the 37 papers published in 1983, and in 108 since its publication.

Two core papers identify each of the three smaller 1983 research fronts related to celery. Research front #83-2593 concerns "Soil salinity, irrigation and fertilizer effects on crop yield of celery." It was identified by two core papers from the US Salinity Laboratory, Agricultural Research Service, USDA, Riverside, California. One, from 1974, is by L. Bernstein and colleagues,[44] and the other, published in 1977, is by E.V. Maas and G.J. Hoffman.[45] This illus-

Figure 3: Higher-level cluster map for "Physiology, resistance to disease, and seed germination in plants" (cluster #217).

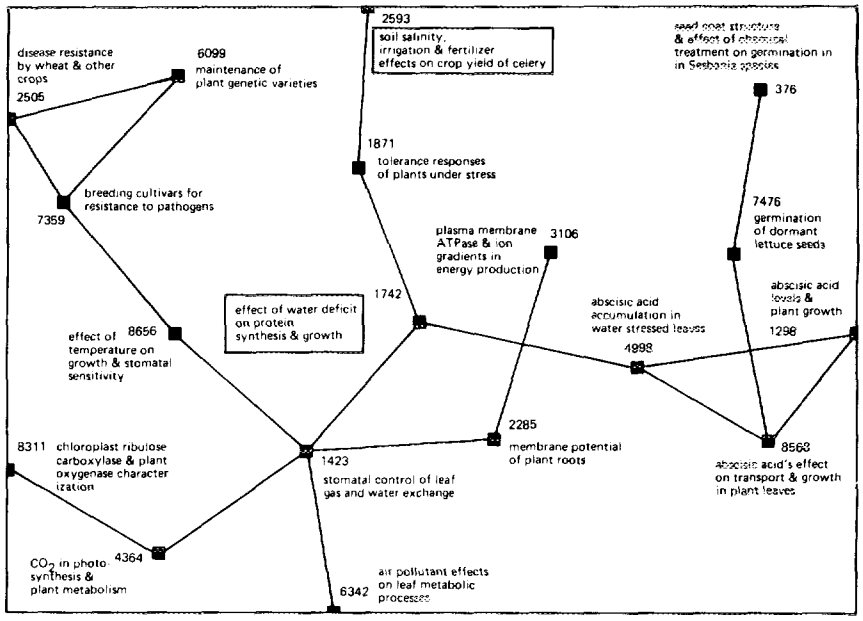
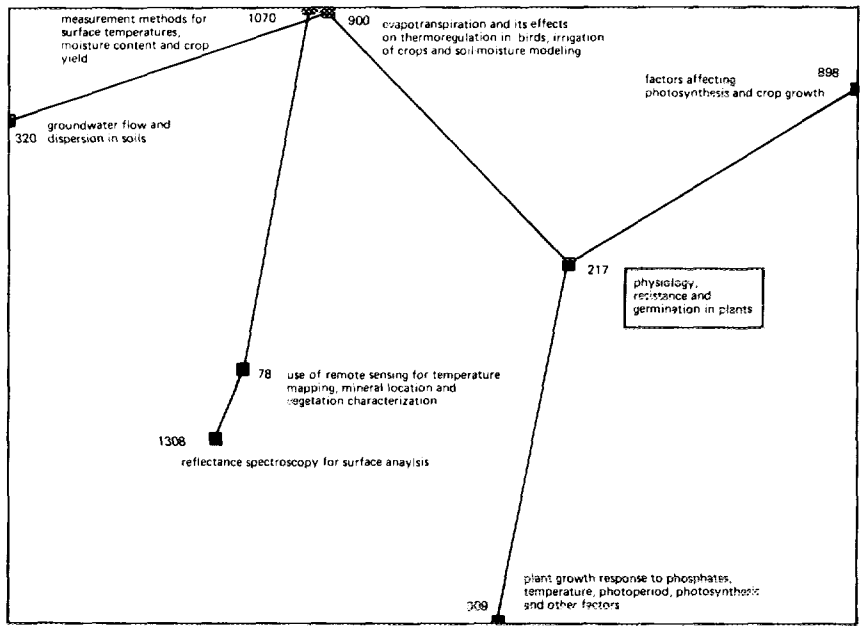


Figure 4: Multidimensional scaling map for eight clusters concerning "Measurements of vegetation patterns, plant growth and crop yields" (cluster #34).



trates how two earlier papers can be used to identify the current literature. The latter paper[45] is also one of five core papers that identify the expansion of this front in 1984 (#84-1465) with the addition of four more papers.

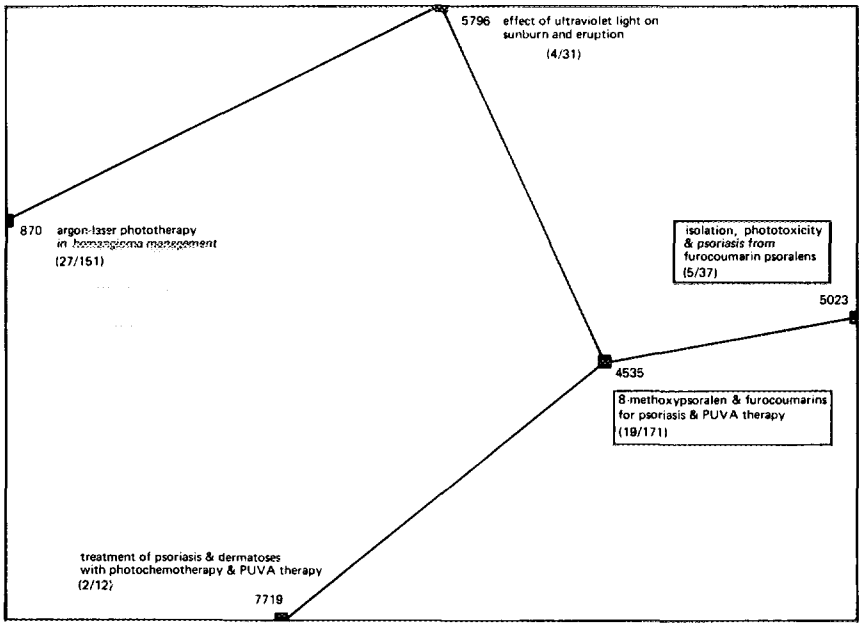
A pair of papers, one by W. Heydecker and P. Coolbear, School of Agriculture, University of Nottingham, England,[46] and the other by B.E. Michel and M.R. Kaufmann, Department of Botany, University of Georgia, Athens,[46] are core to the current research on "Effect of solutions on seed germination of plants including celery" (#83-7245). The Heydecker/Coolbear[46] and the Michel/Kaufmann[47] papers also help identify the 1984 research front, #84-7205, involving the effects of ethanol on seed germination.

Front #83-9097, "Effect of seedling emergence time, soil composition and other factors on the maturity and yield of carrots and other vegetable seeds," is identified by two papers[48,49] published by the National Vegetable Research Station, Wellesbourne, Warwick, England.

Figure 3 is a higher-level map for the cluster (#217) of 18 research fronts on "Physiology, resistance to disease and seed germination in plants." The research front designated by point 2593, involving soil salinity, is one of the many fronts linked together through protein synthesis (#1742). Figure 4 shows the even higher-level cluster (#34) named "Measurements of vegetation patterns, plant growth, and crop yields." This map includes cluster #217, as well as seven other clusters. By looking at the map in Figure 4, we can see how cluster #217 relates to other important areas of agricultural research.

The amount of research published on celery *per se* is not large. Were you to search under the term in the *Science Citation Index®* for the past 10 years, you would find about 25 papers per year. There seems to be very little current research that would support any of the

Figure 5: Higher-level map of cluster #397, "Phototherapy in the treatment of psoriasis and dermatoses." Numbers in parentheses indicate the number of core/citing papers in each research front.



wilder claims for celery, but certainly the implications for dermatology of the studies arising out of the understanding of its toxic effects will have great implications.

The literature on the psoralens is already quite large and would represent a major departure from our main theme. However, the 1983 secondary-level map, "Phototherapy in the treatment of psoriasis and dermatoses," shown in Figure 5, gives us some idea of its connection to the more central theme of psoriasis investigation. The map links five separately identified fronts in modern biomedical research. We have shown, in parentheses, the number of core papers and citing literature for 1983 that could have been listed, but were too numerous to mention here. Note that #83-4535 and #83-5023 from Table 1, which we discussed earlier, are on the far right of this map.

* * * * *

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