Review article

The Hoxsey Treatment: Cancer quackery or effective physiological adjuvant?

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I. INTRODUCTION

In 1983 Steve Austin, the assistant professor of nutrition at the National College of Naturopathic Medicine (NCNM), returned from a preliminary survey of the alternative cancer treatment centers in Tijuana, Mexico. He informed me of the unexpected results that he had observed at the Bio-Medical Center which utilized the controversial Hoxsey tonic in the treatment of cancer. Dr. Austin indicated that his initial impression was that the Hoxsey treatment performed as well as or better than the other methods utilized at the Tijuana cancer clinics. I had recently completed my two-year postgraduate certification at NCNM in general practice and botanical medicine and was an instructor in botanical medicine at the college. This sparked my interest in the rationale behind using a herbal formula in treating cancer. He encouraged me to visit the clinic and make my own assessment.

Over the next several months I read Harry Hoxsey's book, You Don't Have To Die (1956), and learned what I could about the tonic and its activities. Hoxsey had been engaged in continual conflict with the A.M.A., F.D.A., and other medical and legal authorities throughout his adult life over the use and promotion of his treatment. In an interview for Man's Magazine Hoxsey claimed that "our files show we cure about 85% of our external cases, and about 25% of the internal. In cancer of the breast our cures range between 50 and 60%." His determination and court battles led to much publicity and attracted many patients to his method, while winning for him the description by the A.M.A. as "the outstanding cancer quack in the United States."(1)

With this background I visited the Bio-Medical Center for eight days from January 30 to February 8, 1984. Seven of these days were spent entirely at the side of Mildred Nelson. Mildred is the nurse who had worked for Hoxsey since the 1940's and in 1963 moved the clinic to Tijuana. She has since provided the tonic to patients and treated all of the external cancer cases herself. During my visit I tried to clarify several issues: what exactly is included in the Hoxsey treatment, how it influences cancer, how patients undergoing treatment are handled, and the potential benefits and limitations of this therapy. This paper addresses my assessment of these issues based on experience at the clinic and study before and after my visit. I will address as specifically as possible some of the pertinent issues involving this approach.

II. THE INTERNAL MEDICINE (HOXSEY TONIC)

The secrecy surrounding the composition of this formula and the variations in different published lists of its components continues to confound those who attempt to evaluate its effects. As the legend goes, Harry's grandfather raised horses in Kentucky in 1840 when one of his horses developed a cancerous lesion. After he put it out to pasture to die, the horse consistently browsed in one corner of the pasture on certain plants, and eventually the lesion was healed. Then his grandfather picked these plants and prepared a brew with which he had success in treating other sick horses. The ingredients were kept a secret and handed down to his son, John C. Hoxsey, who practiced as a veterinarian. John Hoxsey began treating neighbors who had cancer, using the secret tonic internally and chemical preparations externally.(1,2) According to a local doctor John identified as cancer all verrucous lesions that he treated. (3) When he died in 1919 of cancer he passed on the formula for these remedies to his 18-year-old son Harry. (1,2,4) In the early 1920's Harry began publicly treating cancer patients in Taylorville, Illinois. (1,3) The criticism toward Hoxsey's internal medicine at that time included the formula being kept secret. Medical authorities suggested that tertiary syphilis patients might be misdiagnosed and given an iodide preparation as well as local treatments to give the appearance of curing cancer. (3) This is the first indication of identification of a component of the Hoxsey tonic.

In a 1949 libel case won by Harry Hoxsey after he had moved his cancer clinic to Dallas, Texas, the court ordered Hoxsey to produce written formulas for his remedies. At that time Hoxsey listed the following ingredients in his internal medicine: potassium iodide, *Zanthoxyllum fraxineum* (prickly ash bark), *Rhamnus frangula* (buckthorn), *Rhamnus purshiana* (cascara sagrada), *Medicago sativa* (alfalfa), *Trifolium pratense* (red clover), and honey drip cane syrup. He defended the use of these ingredients by noting their presence in the homeopathic pharmacopeia. One of Hoxsey's nurses testified that she helped prepare the internal tonic by combining 4 oz. each of potassium iodide and cascara to one gallon of water. Chemical analysis revealed that the brownish-black internal medicine contained about equal parts potassium iodide and cascara in about 96% water. Another remedy used was a pink lactate solution. The court findings stated "the respondents ... subtracts and changes the basic elements of the two medicines as indicated, in the judgment of the Medical Director of the clinic when indicated by the examination of the patient, but that no such prescription accompanies shipments made in interstate commerce to the doctors in other states who are using the Hoxsey method, nor does the same appear upon the bottles or receptacles of the medicine."(4) A case filed in 1950 under the Federal Food, Drug and Cosmetic Act resulted in a 1953 court injunction enjoining Hoxsey from delivering his medicines via interstate commerce. This included the pink mixture containing potassium iodide and elixir lactate of pepsin. (5)

By 1954 the dark brown liquid Hoxsey medicine carried a label listing the following ingredients in each 5 cc: potassium iodide (150 mg), licorice (20 mg), red clover (20 mg), burdock root (10 mg), stillingia root (10 mg), berberis root (10 mg), poke root (10 mg), cascara amarga (5 mg), prickly ash bark (5 mg), and buckthorn bark (20 mg). The dosage instructions were to take one teaspoonful (5 cc) after meals and at bedtime. The Bureau of Investigation for the A.M.A. noted that of these ingredients, only potassium iodide had any recognized therapeutic activity at that time. Potassium iodide was used as an expectorant in cough remedies at twice the dose indicated on the Hoxsey label. (5) This list of herbs is essentially what Hoxsey gave in his book two years later, though without the proportions. What the A.M.A. as well as Hoxsey failed to announce was that a remarkably similar formula (without the potassium iodide and buckthorn and with proportionally more cascara amarga and prickly ash) had been in-

cluded in the National Formulary (NF) 5th (1926) and 6th (1936) editions as an official remedy known as Compound Fluidextract of Trifolium. The dosage used for this medicine was one fluidram (4 cc). Frequency of dose was not indicated. (6,7) This calls into serious question the story that the current tonic formula originated with his grandfather's horse, especially since several of the plants cannot be found growing in the Midwest.

The origins of the Trifolium Compound go back to the 19th century. In 1890 Parke, Davis & Co. produced a Syrup Trifolium Compound that approximated the modern formulas except it contained potassium iodide and no licorice. The dose was from 1-2 fluidrams (4-8 cc) three times daily. For many of the newer Parke-Davis remedies authorities were quoted so that "the value of the statements given may be determined by the professional eminence of the originators." They noted that the syrup was recommended by a Dr. Rush, after much clinical experience, as a superior alterative for general use and when prescribed in cases of secondary syphilis acted promptly and unequivocally. (8) No other information on Dr. Rush was given. Several decades later in advertisements appearing in medical journals, Parke, Davis & Co. identified the Syrup Trifolium Compound as a long-established success prescribed in every civilized country in the world. It was described as "one of the most valuable alteratives known to the medical profession ... widely prescribed in scrofulosis and cutaneous affections ... in secondary and tertiary syphilis, acting as a tonic to the digestive, assimilative and excretory organs." It was also used as a vehicle for inorganic medicines and was available with or without cascara sagrada. (9)

The Extract of Trifolium Compound was described in 1898 in King's American Dispensatory, the foremost compilation of medicines used by Eclectic physicians. This pharmaceutical preparation was deemed a specialty of the Wm. S. Merrell Chemical Co. of Cincinnati (now part of Marion Merrell Dow, Inc.). The combination was noted for "the alterative, tonic, and eliminative properties of the recently expressed juices of extracts from fresh or green plants with potassium iodide." Extract Trifolium Compound was intended for use in syphilis, scrofula, chronic rheumatism, glandular and skin conditions. Its ingredients were the same as for the current formulas, but with the addition of potassium iodide and *Podophyllum peltatum*. The latter was at one time considered the eclectic calomel because of its widespread use. (10) Though *Podophyllum* was eventually dropped from the formula, it is interesting that the resin constituents podophyllotoxin alpha- and beta-peltatin were later found to have potent antitumor activity (11) and a derivative is now used in the treatment of human cancers.

Since Hoxsey identified one constituent in his book simply as cascara, this component has taken on added significance in the minds of some herbalists as though it were the key ingredient. The varying lists that Hoxsey identified as his tonic include both cascara sagrada and cascara amarga. Cascara sagrada is the Spanish term for "sacred bark," the name used for *Rhamnus purshiana* when it was introduced by the eclectic physician J.H. Bundy in 1877 and its fluidextract first produced by Parke, Davis & Co. in 1878.(12) Cascara amarga is Spanish for "bitter bark" and has been applied as a common name to a number of Latin American plants. It is Cascara amarga that appears in the older Parke, Davis & Co., Merrell Chemical Co., and the current "NF" formulas where it is also identified as Honduras bark. Parke, Davis & Co. (1890) stated its source was an unidentified *Picramnia* species. It was said to be an alterative and almost a specific for syphilis. (8) King's American Dispensatory (1898) says cascara amarga was recommended for syphilitic affections and was "supposed to come from a species of *Picrasma*" (Fam. Simarubaceae) other than *Picrasma excelsa* (commonly known as quassia wood).(10) The NF 5th ed. (1926) describes cascara amarga as the dried bark of an undetermined species of *Picramnia* (Fam. Simarubaceae). (6) A popular herbal published in 1931 identified Cascara amarga as *Picramnia antidesma* from Jamaica and South Guiana and said it was used as a digestive tonic in diarrhea and dysentery. (13) The 6th ed. of the NF (1936) then proclaimed that cascara amarga was the dried bark of *Sweetia panamensis* (Fam. Leguminosae). (7) To cut through the confusion I asked Mildred Nelson what was the true source of the cascara in the Hoxsey tonic. She replied that they had used Cascara amarga for a number of years, but it became impossible to obtain. Thereafter they substituted Cascara sagrada, and the tonic worked just as well (See Table I).

In 1956 a public warning against the Hoxsey cancer treatment issued by the commissioner of the F.D.A., George Larrick, identified the Hoxsey medicines as consisting of black pills and brownish-black liquid which both contained the 1954 list but included the substitution of Cascara sagrada for the Cascara amarga. He also identified red pills as containing potassium iodide, red clover, stillingia root, poke root, buckthorn, and pepsin and the light red liquid containing potassium iodide in elixir of lactated pepsin. (14) These appear to be adaptations being made to fit different patient needs. Exact individual prescription adjustments remain unclear. A publication on alternative cancer therapies identifies red "lactab" pills that are the same as the black pills plus 0.1 mg pepsin but without licorice, burdock root, and cascara sagrada. It also mentions yellow tablets having the same ingredients as the black pills except for 4.85 grains of iodized lime being substituted for the 75 mg of potassium iodide. (15)

Since 1963 when Mildred Nelson moved the clinic to Tijuana, Mexico, she has only used the liquid form of the formula. She explained to me that this was because the pills did not work as well since the powdered herbs were too hard for patients to digest and absorb. She prepared the liquid tonic by infusion of the herbs. She also said that no alcohol was used in preparing the tonic since alcohol nullified the effects of the tonic in the body. (16) The NF formula used the dried, powdered plant parts extracted with one part ethanol and three parts water (6,7). Since the Hoxsey tonic contained no alcohol it was preserved by refrigeration, and if it soured the patient would be sent a new bottle. (16) The iodide undoubtedly helped to prevent bacterial or yeast fermentation.

When I asked Mildred about the list of herbs that Hoxsey gave, she replied that he was required by law to provide a list, so that was the list he gave them. This seemed to imply to me that he may not have been forthright in sharing the secret tonic formula, though the first list given in court appeared close to what his grandfather's horse might actually have consumed in a Midwest pasture. Mildred mentioned changing the formula in some cases, adjusting it every way she knew how, to meet the needs of individual patients. (16) The instruction sheet given to patients at the clinic says that the tonic varies in different cases. (18) The Tijuana clinic reportedly no longer mentions prickly ash bark and buckthorn bark in the list of ingredients from patient literature but specifies potassium iodide and herbs, licorice, red clover, cascara, burdock root, berberis root, poke root, and stillingia root. (17)

The tonic that Mildred Nelson now gives patients is a concentrate. This is the same form that Hoxsey supplied to physicians and practitioners that used his tonic in the late 1940s. (4) Patients are advised to mix one part tonic with seven parts tap water. Mildred is

opposed to the use of distilled water since it lacks essential trace minerals that are important for metabolism. The diluted tonic is preferably to be taken in one third glass of water, fresh grape juice or other fresh juices (not canned or frozen), or in milk, coffee, or herb teas. The dose of the dilution for children is from 5 drops to one half teaspoon taken four times daily. The usual adult dose is one teaspoons four times a day (16,18). Up to five teaspoons four times daily may be indicated for certain individuals. The tonic is taken for at least five years and then every spring and fall thereafter for 3-4 months each. The instructions for larger doses for adults begin with one teaspoon per dose four times a day for three weeks. In the fourth week one of the doses is increased to two teaspoons, in the fifth week two daily doses are two teaspoons and two doses remain one teaspoon. The sixth week two teaspoons are taken three times daily and one teaspoon once daily. From the seventh week onward two teaspoons are taken four times a day. However, most patients cannot tolerate high doses and reach their own personal tolerance level prior to this (16). Nausea, loss of appetite or weakness may be noticed in some cases. The potassium iodide my cause mild symptoms of iodism to appear. These side effects begin with watering eyes, a runny nose, and/or pimples on the shoulders, face and forehead. If any of these symptoms cause significant discomfort, use of the tonic is stopped for 1-2 days and then resumed at half the dose and gradually built back up to tolerance levels. (18)

Controversy over the Ways and Means of Cancer Control

In addressing court findings of 1950 that "the respondents' (Hoxsey's) treatment is not injurious; some it cures, and some it does not cure, and some it relieves somewhat," the Bureau of Investigation of the A.M.A. responded," there is no known liquid medicine which cures internal cancer."(4) The A.M.A. focused its denunciation on the internal tonic. In their review of the ingredients in the Hoxsey tonic, they stated emphatically, "Any such person who would seriously contend that scientific medicine is under any obligation to investigate such a mixture or its promoter is either stupid or dishonest."(5) Since these statements were made in a day when conventional medicine denied the association of diet with cancer and ignored the link between smoking and cancer, this author believes that such judgments were expressions of bias rather than knowledge. Presumably, the medical establishment was sincere in its belief that it held the only hope for effective treatment of cancer in its many forms. In 1956 the F.D.A. commissioner, in a press release on the Hoxsey treatment issued by the U.S. Dep. of Health, Education, and Welfare, stated, "Cancer can be cured only through surgery or radiation."(14)

The use of internal medicine by Hoxsey to treat cancer was based on the belief that cancer was a consequence of abnormal cellular metabolism and chemistry of the blood (1,17). This was the belief of the irregular eclectic medical doctors at the turn of the century when the Trifolium Compound remedies became popular for treating a variety of generalized conditions. According to the renowned doctor, Eli Jones, "The Eclectic school of medicine was the pioneer in the successful treatment of cancer by internal medication ... By my method of treating cancer as a blood or constitutional disease (as I was taught in the eclectic college over forty years ago) I have cured 80% of the cases of cancer which have come under my treatment. I honestly believe, from my own experience, that 95% of the cases of cancer in our country could be cured by medicine if treated before any operation or the use of x-ray."(19) This surpasses even the opinion of Hoxsey who stated, "If we were to get cases in the first stages of the disease - before metastasis and before the knife and radiation destroy circulation to the affected areas - I feel we could cure 85% of all external and 50% of all internal cases."(1) The medical director of Hoxsey's clinic in 1947 remarked that the extensive destruction due to maximum x-ray and radium treatments remove all hope for the cure of the cancer. Even then he believed the Hoxsey treatment might "limit the further extension of the cancer and keep the patient free from pain," so that "in almost every case the general health of the patient improves."(17) Obviously, we are faced with two entirely different approaches to the treatment of cancer.

The more difficult a condition is to treat, the more numerous are the remedies listed as being used against it. Thousands of simple plant remedies have been used in folk remedies for the treatment of cancer. (20) That herbs in the Hoxsey treatment are among these should come as no surprise. (11,20) In assessing the potential value of the Hoxsey formula in cancer treatments, the current conventional scientific method has been to look at its component plants individually or their isolated constituents in regard to cytotoxic or antitumor activity. (17) While this may or may not help establish some degree of justification based on conventional understanding of cancer treatment, it does not address the intended purpose of using the formula as being a means of normalizing physiologic processes and thereby assisting the body in its control of cancerous growth. According to Hoxsey, "It follows that if the constitution of body fluids can be normalized and the original chemical balance in the body restored, the environment again will become unfavorable for the survival and reproduction of these cells, they will cease to multiply and eventually they will die. Then if vital organs have not been too seriously damaged by the malignancy (or by surgery or irradiation) the entire organism will recover normal health. That, in brief, is the theory of the Hoxsey treatment. We are convinced that cancer cannot be cured successfully as an isolated phenomenon, unrelated to basic body processes. We attempt to get at the roots of the disorder, rather than deal merely with its end result. Our primary effort is to restore the body to physiological normalcy."(21)

The application of the early Trifolium Compound remedies was for the alterative, tonic, and eliminative activity of the combination. (9,10) Tonics, often bitter, were employed to increase the appetite and enhance the processes of digestion and assimilation, thus improving the quality of the blood and the nutrition of the nervous system. Alteratives, known in folk medicine as "blood cleansers," were seen as assisting organs that remove metabolic waste and toxins from the circulation. They were used for chronic conditions in small amounts over prolonged periods. Alteratives were believed to improve the quality of the blood by assisting digestion, improving circulation, and accelerating the processes of elimination, thereby correcting faulty metabolism. The knowledge concerning their action was wholly empiric. (22) Health was seen as a product of the quality of the blood, since the blood brings nourishment to tissues and cells. The cellular waste must also be removed by the venous capillary blood or returned via the lymph fluid to the venous circulation. Cleansing the blood occurs as it is filtered through the emunctories (organs which excrete cellular waste products). These organs include the kidneys, liver, skin, and lungs. While the lungs expel gaseous waste from the blood, the sweat glands of the skin excrete some water soluble substances. The kidneys excrete much of the soluble waste from the blood. However, it is necessary for many compounds to be processed by the liver before they can be excreted. If the liver does not adequately metabolize physiologic or xenobiotic substances, these compounds accumulate and produce toxic symptoms. The liver excretes

Ingredients	1890 Syrup Trifolium Compound (8,9)	1898 Extract Trifolium Compound (10)	1926, 1936 Compound Fluid Extract of Trifolium (6,7)	1949 Court order listing of Hoxsey Formula (4)	1954 Label on Hoxsey Tonic (5)	1956 FDA Public Warning on Hoxsey Tonic (14)	1990 Current listing of Hoxsey Formula (17)
Potassium iodide	8(a)	x(b)		x	150(d)	x	x
licorice root (Glycyrrhizza glabra)			215(c)		20	x	x
red clover blossoms (Trifolium pratense)	32	x	215	x	20	x	x
burdock root (Arctium lappa)	16	x	108		10	x	x
stillingia root (Stillingia sylvatica)	16	x	108		10	x	x
berberis root (Berberis vulgaris)	16	x	108		10	x	x
poke root (Phytolacca americana)	16	x	108		10	x	x
cascara amarga (Picramnia sp., Picramnia antidesma or Sweetia panamensis)	16	x	108		5		
cascara sagrada (Rhamnus purshiana)	0 or 40			x		x	x
prickly ash bark (Zanthoxylum americanum or Z. calva herculis	4	x	30	x	5	x	
buckthorn bark (Rhamnus frangula)				x	20	x	
mayaple root (Podophyllum pelatum)		x					
alfalfa plant (Medicago sativa)				x			
Other			alcohol 17-21%	sugar syrup			
Dose	4-8 cc t.i.d.		4 cc		5 cc q.i.d/		

some of these metabolites along with bile into the intestines where they are hopefully eliminated through the colon along with the waste from undigested food. Certain herbal agents can help facilitate these processes. (23)

Maintaining optimal blood purification especially requires efficient elimination from the bowels. In cases of constipation the reabsorption of waste compounds from the colon contaminates the blood. Toxins produced by intestinal bacteria from the breakdown of undigested protein can also be absorbed. An increased burden of waste excretion then falls on the skin, lungs, and kidneys as toxins accumulate in the blood. When these emunctories do not function adequately, it becomes increasingly difficult to maintain a healthy ecology of the cells. This makes them more susceptible to carcinogens that our increasingly prevalent in our air, water, and food and thereby contaminate our internal environment. As mitotic aberrations become manifest, those cells that thrive best in the altered fluid chemistry are selected to survive. T-lymphocytes and neutrophils in the blood, lymph fluid, lungs, liver, spleen, thymus, and lymph nodes that help destroy mutant cells by phagocytosis and thereby "cleanse the blood" may have reduced efficiency under these conditions. Attempting to enhance elimination and immune function can be done by utilizing a variety of methods and agents including herbs.(23)

This model for the action of alteratives was practically applied by the late 19th-century eclectic prescribers in the treatment of chronic and cancerous conditions. Such was their success that the alteratives were considered to have been among the most useful medicines in eclectic therapeutics. (22) Relying on the most authoritative text of the eclectics, King's American Dispensatory,(10) the pertinent properties and applications of the plants contained in the Hoxsey tonic will be examined in the next section. Further understanding of their activities derived from more recent research will also be addressed. Finally, information regarding anti-tumor research on these plants or their active constituents will be noted to assess their direct effect on cancer cells.

A major controversial aspect of the Hoxsey approach has already become incorporated into conventional cancer therapy. Though medical theorists of Hoxsey's day argued that cancer can not be cured with internal medicine, oncologists now treat a variety of cancers internally with a number of substances derived from plant constituents. Etoposide derived from the podophyllotoxin in *Podophyllum peltatum* is used to treat testicular tumors, small-cell lung cancer, nonlymphocytic leukemias, and non-Hodgkins lymphoma. Vincristine and vinblastine from *Vinca rosea* are used to treat acute childhood leukemia and Hodgkins disease, respectively. Polysaccharides with antitumor and immuno-modulating functions from the mushroom *Lentinus edodes* (shiitake) and the sclerotia of Polyporus umbellatus are being studied for the purpose of potentiating chemotherapy.(17) New possibilites await those who examine creative strategies in treating malignancies.

Effects and Uses of Individual Components of the Tonic

Whatever benefit can be derived from plant remedies individually, separate examination does not adequately represent the effects of a combination since it does not take the synergism of the different components into account. Studying isolated constituents is even more inadequate when a combination of plants is used in a protocol involving other factors such as diet or additional treatment modalities. However, it is necessary to examine the actions of component parts to help appreciate their contribution to the overall effect produced.

TABLE 1 (opposite): Ingredients lists for Trifolium Compound preparations and the Hoxey Tonic. a= grains per ounce; b= amount contained in formula unlisted; c= grams per liter; d= milligrams per cubic centimeter.

Red clover

Since *Trifolium pratense* (red clover) blossoms are proportionally one of the major ingredients, and the alterative formula has in the past been named for this plant, it seems appropriate to examine it first. The eclectics described red clover as an excellent alterative. It was often utilized for the coughs associated with respiratory infections. It was said to unquestionably retard the growth of carcinomata when administered internally for a prolonged period and was given freely to those with a cancerous diathesis. The infusion was taken as frequently as desired or 1-60 drops of a strong tincture (eight ounces of dried flowers to one pint of 50% alcohol) was used.(10)

Water-soluble polysaccharides (insoluble in ethanol) in a red clover crude fraction showed antitumor activity together with chemotactic effects for leukocytes, mostly granulocytic, when administered by intraperitoneal injection in CAF1 mice with peritoneal Sarcoma 37 ascites tumor cells.24 Red clover had no activity in the P388 system. The National Cancer Institute (NCI) tested red clover 94 times. Only one test showed activity, and it was not considered significant.17

Red clover, like alfalfa, contains relatively high yields (up to 1% dry weight which was the same in fresh and oven-dried samples) of the estrogenic isoflavone compounds formononetin and biochanin A.(25,26) These isoflavones have very weak estrogen activity when compared with natural estrone or synthetic DES.(27) Formononetin was shown to have little affinity for estrogen receptors and produced no effect on growth of human breast cancer cells in vitro compared to controls.(28) Phytoestrogens can even act as anti-estrogens to impede the binding of endogenous estradiol by competing for cytoplasmic receptors in estrogen-sensitive tissues.(28,29) Such a relationship has been suggested as being responsible for the low incidence of breast and other female reproductive cancers in Japanese women in Japan where soybean products are commonly consumed. Soybeans contain the estrogenic isoflavone glucoside genistin.(30)

Licorice

Glycyrrhiza glabra (licorice) root was an official medication in the United States Pharmacopeia (USP) from 1820-1970. (31) It was often used as a sweet flavoring vehicle, especially to mask bitter flavors. In addition, licorice was employed from ancient times and by eclectic doctors as a soothing demulcent to lessen irritation in respiratory, urinary, and gastrointestinal complaints. It was commonly administered as a decoction which was not to be boiled over five minutes (10,32).

The pharmacologic activity is ascribed to the constituent glycyrrhizin and its aglycon, glycyrrhetic acid, a pentacyclic terpene. These produce healing of peptic ulcers (32,33) and possess anti-inflammatory activity as well (32,34). The latter effect is believed to be due in part to the inhibition of the enzyme 5 beta-reductase which is important in the metabolism of cortisol and aldosterone in humans. The cortisol then acts in synergism with the glycyrrhizin (35). However, when taken in very large quantities over prolonged periods, the enhanced aldosterone effect may lead in some individuals to dangerously low serum potassium (36,37) or hypertension from sodium retention and increased fluid volume (37). Potassium is supplied as

part of the Hoxey tonic. The amount of licorice used in the tonic combination is apparently insufficient to cause hypertensive problems, since this has never been reported (17). Glycyrrhizin has also been shown to induce interferon production in vivo in mice which can lead to enhanced immune responses (38).

Glycyrrhetic acid has demonstrated antitumor-promoting activity in vivo in mice exposed to topical carcinogens.(39,40) Glycyrrhizin has demonstrated anti-estrogen activity in mice and rats.(41) In addition licorice root has been shown to contain small amounts of the isoflavone formononetin. (42) This could help explain the influence that subdermal injection of USP licorice root had in inhibiting RC mammary carcinoma transplanted in DBA mice. It also inhibited lymphosarcoma 150 in DBA mice. (43) Licorice was inactive in one Sarcoma 37 test system study. NCI tested licorice 19 times, but the activity shown in only one sample was not considered significant. A number of components isolated from licorice including glycyrrhizin and the ubiquitous beta-sitosterol have shown antitumor activity in animal test systems.(17)

Burdock root

Arctium lappa (burdock, formerly identified as *Lappa officinalis* or *L. minor*) root was official in the USP in 1830 and from 1850-1900. (31) It was used by eclectics as an alterative for its diaphoretic, diuretic, and laxative properties. From 4-6 fluid ounces of a decoction of the root was used 3-4 times daily for chronic rheumatic or dermal conditions.(10) Burdock roots have shown antibiotic activity on staphylococci (44) and contain several polyacetylene compounds (45) that are antimicrobial.(46)

Arctium lappa is also known for its inclusion in another herbal combination for cancer called "Essiac."(17) Burdock contains a complex polymer having a molecular weight of about 300,000 that reduces the mutagenicity of mutagens. It is effective against both direct and indirect mutagens.(47,48) Water-soluble polysaccharides from a crude fraction of burdock root, as well as being chemotactic activity for granulocytic leukocytes, have shown antitumor effects against solid sarcoma 37 tumor in CAF1 mice.(24) Methanolic extracts of the fresh root inhibited Ehrlich ascite carcinoma and Yoshima sarcoma in animals. An oily fraction was active against the solid S180 system. The active principle was always found in the water insoluble fractions.(49) A tumor growth inhibiting mixture was also isolated by extraction of burdock root with CH2Cl2 and ethanol.(50) While several independent studies were positive and several negative for antitumor activity in animal systems, the NCI had only 1 test out of 14 that showed activity. This was in the P388 mouse leukemia system, but the antitumor activity was not considered significant.(17)

Berberis root

Some believe this agent to be barberry bark (*Berberis vulgaris*).(17) *B. vulgaris* was official in the USP in 1830 and 1860-1870, while *B. aquifolium* was official there in 1900.(31) The NF of 1926 identified the official *Berberis* in Compound Fluidextract of *Trifolium* as Oregon grape root, consisting of the dried roots and rhizome of species of the section *Mahonia* in the genus *Berberis*.(6) Parke, Davis & Co. used *Berberis aquifolium* in their Syrup Trifolium Compound.(8,9) The Eclectic Dr. J.H. Bundy first introduced this species into medical literature in the late 1870s, and Parke, Davis, & Co. brought it into general use. King's American Dispensatory also identified the plant in Extract Trifolium Compound as *Berberis aquifolium* (taxonomically in the section Mahonia, whereas *B. vulgaris* is not), though it noted *B. nervosa* and *B. repens* of the section Mahonia were often substituted for it in the market. Oregon grape root was extolled by eclectics as an alterative and tonic. It was recommended for syphilis and cutaneous affections. *Berberis* was said to promote secretion and excretion by improving digestion and assimilation, stimulating lymphatic glands, and augmenting renal function. Chiefly, it was used to build up the blood and to treat dyspepsia resulting from inadequate gastric and liver secretions. *Berberis* showed itself valuable in the dyscrasia due to cancerous cachexia, but failed to cure carcinoma. Its dose should be relatively large, and 10-20 drops of the fluid extract was usually given every 3-4 hours.(10)

Berberis extract was shown to temporarily affect gastric acid output.(51) *Berberis aquifolium* and other Berberis or Mahonia species have a number of structurally-similar alkaloids in common, but the chief alkaloidal component is invariably berberine.(52,53) Berberine and other berberis alkaloids stimulate biliary secretion. Berberine produced the greatest effect, tripling bile excretion in one and a half hours.(54) In a clinical trial of 225 patients with chronic cholecystitis, oral berberine before meals eliminated clinical symptoms and changed pathological indices with no side effects. It even produced some positive effects in toxic hepatitis caused by industrial poisons.(55) Berberine has wide-ranging antimicrobial activity against a variety of Gram-positive and Gram-negative bacteria, fungi, and protozoa.(56)

Berberine was shown to be a potent macrophage activator for inducing cytostatic activity against tumor cells in vitro.(57) Berberine inhibited the respiration of ascites tumor 15%58 and inhibited the growth of Ehrlich ascites tumor or lymphoma NK/Ly cells by greater than 50% in vitro.(59) However, when injected intraperitoneally in mice with the same ascites tumors, berberine did not inhibit tumor growth.(59) A *Berberis aquifolium* extract produced by Eclectic pharmacists inhibited RC mammary carcinoma in mice.(43) Barberry (*B. vulgaris*) has shown antitumor activity in several tests, but the NCI reported no activity from its one test.(17)

Poke root

Poke was official in the USP from 1820-1900 where it was been identified as *Phytolacca decandra*,(31) but when the NF made it official again in 1926 its name was listed *P. americana*.(6) The eclectics found the root to be a most valuable alterative for syphilitic and rheumatic complaints. Poke root was favored for infections of the oropharynx and upper respiratory tract. It was noted for benefitting acute and chronic cutaneous conditions and hard lymphatic enlargements. Lymphomas were said to be cured by poke root, and one of its common names was cancer-root.(10) *Phytolacca* was used by the early eclectics for cancers. After 40 years of use Eli Jones considered *Phytolacca* the most valuable general remedy available for the treatment of cancer. He found it especially beneficial in cancers of the breast, throat, and uterus, particularly in patients past middle age. Used alone, he gave five drops of Phytolacca tincture once in three hours.(60)

Poke root loses its medicinal properties over time, so only the green (recently harvested) root should be used to make these fluid preparations,(10,60) though the NF 5th ed. listed the dried root as the part used.(6) Extracts were made with water and alcohol. Poke root is toxic in overdose. Taken internally, from 10-30 grains acts as an irritant to the GI tract, producing nausea and emesis after on hour or so and prolonged cathartic purging. Loss of muscular power, dim vision, diplopia, vertigo, and drowsiness can occur from large, nonfatal doses. Death may result from respiratory paralysis.(10) Toxic-

ity due to poke root ingestion is due to a steroidal glycoside called phytolaccatoxin. Its aglycone, phytolaccagenin, is a b-amarin triterpenoid.(61)

Five separate proteins having mitogenic properties on murine spleen cells have also been fractionated from poke root extracts. These include two major and two minor monomers and a potent polymer.(62) The latter protein was mitogenic for both murine B-cells and T-cells, while the others were only T-cell mitogens.(63) The B-cell differentiation by pokeweed mitogen has been found to be T-cell dependent.(64) Since these finding were all from in vitro studies, it was considered unlikely that activity would be retained in vivo due to digestive breakdown of the proteinaceous mitogens. However, follow-up studies of accidental poisonings of children by poke berries containing these mitogens showed that significant plasmacytosis of peripheral blood occurred in 4 of 5 children with definite exposure. Such exposure can be minimal, since in-vitro studies showed that mitogenicity occurs in even 1:1,000,000 dilutions.(65)

One study using animal test systems showed no antitumor activity of poke root against Ehrlich ascites, Leukemia SN36, and Sarcoma 180 cell cultures. Of the 43 tests on poke root by NCI only the one on the Walker 256 system was considered active, but this test system has been eliminated due to problems with its validity.(17)

Stillingia root

Stillingia sylvatica was listed as an official remedy in the USP from 1840-1910.(31) Known for its unsurpassed alterative influence on secretory and lymphatic functions, *Stillingia* was used for syphilitic symptoms and upper respiratory infections. The dose of the decoction is 1-2 fluid ounces, and the tincture dose is from one half to one fluidram.(10) Eli Jones lists *Stillingia* as another long-time Eclectic internal remedy for cancer.(60)

Due to the irritant properties of its root, it was used only in small doses. In large doses it causes a burning sensation in the stomach with vomiting and purging. Alcoholic extracts of the fresh root are to be preferred, since water does not extract the active components as well. To be of therapeutic value, *Stillingia* must be fresh or recently harvested.(10) The NF states that the root stored for more than two years must not be used.(7) The remedy was valued for its resinous content, and the percentage of resin is diminished the older the dried root becomes.(66) The root sap was analyzed and shown to contain the diterpene ester prostratin. Gnidilatidin and six similar diterpene ester constituents were shown to be topical irritants on the mouse ear.(67) Such irritants were formerly employed to stimulate local circulation and mucosal secretions.(10)

Stillingia sylvatica alcoholic extract was shown to reduce tumor growth in DBA mice with RC mammary carcinoma transplants after a 9-day test period.68 No other independent studies or tests by NCI of Stillingia have been reported, though gnidilatidin has tested positive in animal systems.(17)

Prickly ash bark

The barks of *Zanthoxylum* (sometimes spelled *Xanthoxylum*) *americanum* (also called *Z. fraxineum*) and *Z. clava-herculis* (also known as *Z. carolinianum*) were official in the USP from 1820-1920.31 These barks were considered interchangeable. The bark was used as a tonic, alterative, and diaphoretic. Prickly ash was noted for its stimulation of mucous surfaces which thereby augmented the flow of digestive secretions. It was used in small amounts with other alteratives for rheumatic, syphilitic, and scrofulous complaints to enhance their influence. Used alone, the powdered bark was given in doses of 10-30 grains three times daily, or the tincture was used in doses of one half to one fluidram.(10)

Most analytical research has been done on *Z. clava-herculis* bark. Several lignins and the isobutylamide compound neoherculin have been identified. Neoherculin produces a characteristic burning taste and has shown potent sialogogue and insecticidal effects (69) as well as being ichthyotoxic.(70) Neoherculin is identical with the isobutylamide echinacein found in *Echinacea angustifolia.*(71) The lipophilic isobutylamides from *E. angustifolia* have been shown to significantly enhance phagocytosis by granulocytes in vitro and in vivo.(47) *Z. clava-herculis* bark also contains the benzophenanthridine alkaloids chelerythrine and nitidine.(72) *Z. americanum* bark also contains these two alkaloids along with several pyranocoumarins.(73)

Nitidine exhibits cytotoxicity and has shown high activity in the P-388 and L-1210 leukemia test systems.(74) Chelerythrine was cytotoxic to KB tumor cells in vitro but showed no in-vivo activity against P388 or L1210 leukemias in mice.(75) Five NCI tests of prickly ash for antitumor activity were all negative.(17)

Cascara

Considering the aforementioned evidence, the cascara considered here will be cascara sagrada, the bark of *Rhamnus purshiana* which was official in the USP from 1890-1990.(31) Its tonic laxative activity was used in the treatment of dyspepsia from constipation due to muscular atony of the intestines. It was also used for rheumatism or headaches associated with constipation. It acts effectively without causing cramping or excessive catharsis. Ten drops of the fluid extract are taken after meals, gradually increasing the dose until effective, and then gradually reducing the dose and ending its use.(10)

Cascara's anthroquinone glycosides are its major active constituents, since the sugar moiety protects the anthroquinone from oxidative breakdown, though the aglycones that are present act synergistically.(76) The glycosides are cascarosides A and B, chrysophanol glucoside, aloe emodin glucoside, and rheum emodin glucoside,(77) while the aglycones in cascara bark are anthranol, chrysophanic acid, aloe emodin, and emodin.(78) Cascara increases peristalsis and fecal hydration.(79) Its active constituents can be passed through breast milk.(80) Emodin has been shown to both stimulate intestinal activity in vitro and act as a CNS depressant and analgesic in vivo in animal test systems.(81)

Aloe emodin produced tumor-inhibiting activity against P-388 lymphocytic leukemia in mice. This effect was in contrast to previous tests with this compound due to the types of solvent used.(82) The official (USP) extract of cascara sagrada bark inhibited the tumor growth in tumor-bearing eggs in a 24-hour test period and RC mammary carcinoma transplanted in mice after 10 days.(43) No antitumor activity was found using the powdered bark in a test against Sarcoma 37 cells. Sixteen NCI tests were all negative for antitumor activity.(17)

Buckthorn bark

The bark of *Rhamnus frangula* was official in the USP from 1820-1830 and 1880-1910.(31) The dried bark acts as a laxative and was used in cases of chronic constipation. A dose of 20 drops of the fluidextract 1-3 times daily was the usual dosage. A single teaspoonful dose at bedtime acts as a rapid cathartic. The fresh bark produces nausea, colicky pain and violent emeto-catharsis.(10)

The major anthroquinone constituents of *R. frangula* are frangulin A and B, glucofrangulin A and B, and emodin glycoside.(77)

R. frangula contains about half as much total emodin as cascara sagrada.(83) The emodin has shown laxative and analgesic properties in animal models.(81)

Aloe emodin derived from an ethanol-water extract of *R. frangula* has demonstrated activity in mice with P-388 leukemia though it had previously tested inactive against L-1210 leukemia in mice.(82) NCI tested buckthorn 3 times in animal studies, and antitumor results were all negative.(17)

Potassium iodide

In small doses potassium iodide was used by eclectics as an alterative and diuretic. The iodides are rapidly eliminated by salivary and broncho-pulmonary glands as well as the kidneys. In liquifying mucus secretions of the respiratory tract potassium iodide has had its most frequent application as an expectorant. In addition it was a common remedy for goiter and syphilitic symptoms.

Though commonly tolerated in very large doses, even small doses can produce reactions in certain individuals, particularly where kidney function is compromised. Besides the ordinary reactions mentioned previously, sensitive persons may experience vomiting and purging, fever, cramps, palpitation, emaciation, various cutaneous lesions, and sometimes even death. Usually the symptoms pass after its use is stopped. Potassium iodide can also pass into breast milk and produce emaciating effects on suckling infants.(10)

DISCUSSION

The reasons for the secrecy surrounding the tonic formula are documented in Hoxsey's book. His reasons included the possibilities that its application would be limited and sales would be monopolized and/or controlled by unscrupulous business interests to maximize commercial gain. Through his secrecy he maintained his monopoly and control, but expatriation limited its availability. It seems that the secrecy also served for a period of time to protect the public from inadequate imitations. The compounding and application of the tonic require sufficient expertise, since the results can depend on appropriate processing and modifications. A number of "Hoxsey-like" products have arisen since the time Hoxsey published the list in his book. Many available to the general public lack important components and/or are made from inferior quality crude herbs. Potential patients then become simply customers who are provided with very little practical information about proper use, if any, and no supervision whatsoever. As a result many may utilize such products believing them to be adequate to supplant the Hoxsey treatment or approaches conventional medicine has to offer. In the meanwhile Hoxsey's treatment remains available, but only to those who can reach the clinic.

Besides uncertainty about the exact formula(s) used and the proportions of the plant extracts in the tonic, other difficulties exist in attempting to reproduce the tonic without further information being supplied. To retain the activity of certain herbs, it is also necessary that their extracts be made from fresh or recently harvested and dried plant sources. This has been stressed in particular for poke and stillingia. The extracts used in the production of Extract of Trifolium Compound with the exception of prickly ash were from fresh or green plants or recently expressed juices. Much of the therapeutic constituents can be lost during the processes of drying or storage. On the other hand certain herbs such as cascara sagrada and buckthorn bark cannot be used fresh but need to be dried and aged to allow conversion of compounds that produce side effects. Often the blame for lack of efficacy of remedies was placed by eclectics on the poor quality of many of the commercial extracts that were widely available.

The solvent used also affects the content of constituents in the extract. For certain herbs the Eclectics expressed a preference for water extracts (infusion or decoction), for example burdock root, and for alcoholic extracts of others such as stillingia. The efficacy of medicinal extracts of herbs is based upon the active constituents being soluble and preserved in the solvent used. Since water and alcohol have different solvent and preservative capabilities, and since the historical variations of the formula have both included and excluded alcohol, the types of constituents and the activity of the extracts would vary somewhat. For example, the polysaccharides from red clover and burdock and the proteins from poke would be soluble in water but would precipitate in concentrated alcohol. Resinous substances such as those in *Stillingia*, the lipophilic isobutylamide from prickly ash, and the beta-sitosterol in licorice root (and many other plants) are only slightly soluble in water. While alcohol acts as an excellent preservative, organic compounds in water are easily hydrolyzed and sugars are subject to fermentation. Application of pharmaceutical principles in the manufacture of herbal extracts can be as relevant as the therapeutic principles used to prescribe them.

Based upon evidence from independent research, the individual components reported to be in the Hoxsey tonic have a variety of effects on physiologic function. The tonic and alterative claims by eclectics have been relatively substantiated if they are taken to mean an increase in digestive secretions (berberis, prickly ash), cholagogue activity (berberis), laxative effect (cascara, buckthorn), or immunomodulating activity (licorice, berberis, poke, prickly ash). Other influences include estrogen inhibition (red clover, licorice), thyroid stimulation (potassium iodide), antimicrobial activity (burdock, berberis), and anti-inflammatory effects (licorice). These combined effects could help improve cellular nutrition and metabolism and enhance elimination of waste, relieve inflammatory conditions, and improve resistance against infections as was claimed for the Trifolium Compound alterative formulas. These formulas have been applied to treat a variety of mainly chronic conditions. Mildred herself said that she once took the tonic for a kidney condition which was thereby resolved.

Though not cancer-specific in its therapeutic activity, evidence exists that the tonic components produce some direct effects on malignant processes. Constituents of licorice and burdock inhibit the effects of tumor promoters and mutagens, respectively. All of the plants of the Hoxsey tonic or certain of their active constituents have shown some degree of antitumor activity in vitro in human cancer cell-culture studies or in vivo in animal systems. However, neither type of result can be directly extrapolated to humans. They are only useful as a screening method to determine the possibility of clinical antitumor activity. In the same regard practically all of the plants have failed to show activity in similar tests performed in vitro on other cell cultures or and in vivo in other animal studies. This does not rule out the possibility that the plants and their components can indirectly influence tumors through human physiological mechanisms that are not present in vitro or in the different animal species used. It mainly shows a lack of direct cytotoxic or antitumor activity on particular types of cancer cells. However, cancer does not exist in isolation in the body as cells do in a petri dish, and correlation between species is unreliable in negative as well as positive test results. Scientific assessment of clinical trials is the only legitimate means of making an accurate determination of therapeutic effect.

III. EXTERNAL APPLICATIONS AND SUPPORTIVE THERAPIES

The Yellow Powder and Red Paste

Though Hoxsey's book mentioned a clear liquid (trichloroacetic acid) being applied as an escharotic, its use has been abandoned.(17) The first report in the medical literature on Hoxsey referred to his use of an escharotic powder or paste with arsenic as the base. It was claimed by the A.M.A. that some early patients bled to death as a result of the arsenic eating into blood vessels.(3) In the 1949 libel trial a case was described in which a woman died of heavy metal poisoning 10 days after application of the powder was made on a compress under an incision in her breast. It was during this trial that Hoxsey was ordered by the court to list the ingredients to his medicines. At this time he gave the following ingredients for his yellow powder used in external treatments: talc, flowers of sulphur, arsenic trisulfide, sweet elder *(Sambucus canadensis)*, magnolia flower (*Magnolia glauca*), blood root *(Sanguinaria canadensis)*, and antimony trisulfide.(4) This list apparently combined the ingredients of his yellow powder with some of those from the red paste. In his book Hoxsey described the yellow powder as containing talc, sulfur, yellow precipitate, and arsenic sulfide.(17) When asked about the missing herbs, Mildred Nelson insisted that the powder never contained elder or magnolia flowers. She said the yellow precipitate was USP sulfur. Sometimes the yellow powder was mixed with KY gel to make a yellow salve that was applied. Other times the powder was sprinkled or blown onto an open lesion by using an insufflator.(16)

"Additional Hoxsey formulas" provided by the publisher of a book on alternative cancer treatments included several different proportions for the ingredients of the yellow powder. At one time the "famous yellow" was said to contain one part arsenic sulfide yellow precipitate, two parts USP sulfur, and three parts talcum powder which must be very thoroughly mixed together. The other formula was less concentrated and was supposedly so harmless it could be used in the eye. It contained one half ounce yellow arsenic, two ounces of sulfur, and six ounces of talcum which also must be thoroughly mixed.(15) Mildred expressed displeasure to me about this publisher, saying she used the "old" powder formula.(16) The story about the use in the eye may have come from the Man's Magazine interview when Harry Hoxsey theatrically washed his eye with a strong solution of a yellow powder and then swallowed a heaping teaspoonful to demonstrate that the A.M.A. was wrong in claiming that his "dangerous escharotic" destroys normal tissues and causes fatal hemorrhage.(1)

Harry Hoxsey's and Mildred Nelson's remarkable claim for the yellow powder is that it does no harm to normal tissue but only destroys cancerous cells.(16,17) Observing Mildred handling the powder and various moist preparations made with it day after day without taking care to remove it from her own skin when it came in contact demonstrated her belief that it was not harmful with that type of exposure. She also pointed out another feature of the effect of the yellow powder on cancerous tissue.(16) After the cancer necrosed and fell away from the skin "like the pit from a peach," the healing tissue would in some cases fuse together to leave a linear scar that had the appearance of a thin incision.(1) Such a scar was shown to me on the right temple of a patient who had been treated with the yellow powder there for a basal cell carcinoma. The patients I observed did not complain of pain or excessive tissue destruction from the yellow powder.(16) Eli Jones insisted that he never used arsenic locally in the treatment of cancer since it was too painful and too dangerous, though he did not specify which compound. He mentioned that is was used for many years by conventional doctors, especially a formula created by a Dr. Marsden who made of a paste with arsenic and acacia gum which was applied locally.(60) Hoxsey's yellow powder was said to work better on cervical cancer than the red salve treatment described by Eli Jones and used by some naturopathic doctors, but it requires frequent application.(16)

The red paste used in the Hoxsey treatment was first described by Hoxsey in his book. It was said to contain zinc chloride, antimony trisulfide, and bloodroot. The red paste is an escharotic that destroys normal and cancerous tissue with which it was kept in contact.(17) When the eschar fell off, the red paste would leave a unique smooth scar that Mildred said she could recognize anywhere.(16) Similar pastes had been used for at least a century. Bloodroot *(Sanguinaria canadensis)* was used by Cherokee Indians for breast cancer. An American doctor, J.W. Fell, said he learned of its application from them and included it in salves, publishing his formulas in 1857. Sanguinarine and chelerythrine are alkaloids found in bloodroot that have shown antitumor activity in reducing the growth of Ehrlich carcinoma and Sarcoma 37 in mice.(11) Bloodroot contains another alkaloid, sanguidimerine,(84) that was active against Eagle's 9KB carcinoma in vitro though it was inactive against Walker 256 carcinosarcoma in rats.(85) Sanguinarine and chelerythrine have demonstrated antimicrobial activity in vitro against *Staphylococcus aureus, Klebsiella pneumoniae, Mycobacterium smegmatis*, and *Candida albicans*.(86) Sanguinarine also inhibited Trichomonas vaginalis in vitro and was effective in vivo against *Staph. aureus* and *Escherichia coli* pyogenic infections when applied locally to rabbits.(87)

In 1900 Dr. James McDonald described a topical paste for cancer containing zinc chloride, *Sanguinaria* root powder, rye flour, bayberry wax, and Conium solid extract mixed with a water extract of red clover. This was used together with an internal formula consisting of fluidextracts of burdock, *Phytolacca*, and other alteratives.(88) Dr. Eli Jones used several similar escharotic pastes. The one used in most cases for deeper cancers of the breast, lip, hand, foot, arm, or back included solid extract of *Sanguinaria*, zinc chloride, starch, and red saunders (Pterocarpus santalinus wood). He would use his pastes in conjunction with an internal alterative formula and other varying remedies depending on the case including homeopathic medicines.(60) In the 1940s and 1950s Dr. Perry Nichol's cancer sanatorium in Savannah, Missouri, used an escharotic paste. The escharotic was described as a double compound about four times the strength of zinc chloride plaster, or the arsenical or Marsden's paste. A patient remarked that the treatment did not cure cancers, it killed the cancers. The chances for survival in severe (not incurable) cases was about 50%, while for early stage disease it was around 75%.89 My grandfather was successfully treated there for a cancerous lesion on his ear; a hole through the pinna was a welcome reminder for 30 years of the efficacy of this therapy.

During the 1930s Dr. Frederic Mohs from the University of Wisconsin Medical School developed a method of removing accessible cancers by a microscopically controlled method of chemosurgery. In his technique he utilized a fixative compound for in situ preservation of tissue structure that could be examined under a microscope after excision for the purpose of mapping tumor extensions. The fixative was zinc chloride in a base with consisting of stibnite (antimony trisulfide) as a "permeant" to facilitate infiltration of the zinc chloride and *Sanguinaria* canadensis as an "agglutinant" to keep the zinc chloride evenly dispersed in the base. The formula he used was antimony trisulfide (80 mesh sieve) 40.0 grams, Sangui-

naria 10.0 grams, and zinc chloride saturated solution 34.5 cc. By repeated applications and excisions following microscopic mapping, the tumor could be precisely identified and completely eradicated with minimal damage to normal surrounding tissue. Primary basal cell and squamous cell carcinomas were effectively treated, with sarcomas, melanomas, and other malignant tumors also susceptible to this method. Of 440 malignant lesions treated by this method 93% were cured.(90) The size of the primary lesion determine the prognosis using Mohs treatment of basal cell and squamous cell carcinomas with 97.4% and 85.6% cured overall, respectively.(91) By 1962 the formula of the fixative paste had been changed to 40 grams of stibnite, 2.5 grams *Sanguinaria*, and 20 cc of saturated solution of zinc chloride. In some patients considerable local pain was associated with the application of the fixative material.(92) The pain was allayed by giving the patient 10 mg of morphine every three hours as needed.(93)

Possibly due to the success of the Mohs technique, the A.M.A. ceased denying that Hoxsey's treatment cured external cancers and admitted its efficacy but described it as archaic. Because of the problems with local pain and various time-consuming aspects, the fixative paste was eventually excluded from the Mohs technique.(17) Tests with a topical application of zinc chloride and NDGA, the active lignin from chaparral *(Larrea tridentata)*, reduced or suppressed B-16 melanoma and Sarcoma-180 tumors in mice and increased the survival time.(94) There has been evidence in several human cases that chaparral has antitumor activity against melanoma.(17) Currently, an escharotic salve containing zinc chloride and chaparral extract but lacking FDA approval is being marketed from the Bahamas. It is advocated as an effective treatment of external cancer after one application. While its manufacturers state "it is often a good idea to seek out a competent health care professional," unfortunately it is being sold to individuals for home treatment.

External Treatments and Local Applications

Topical lesions were washed before treatment with a pine oil and soap solution which acted as a disinfectant and controlled the putrid odor of some external cancers. Mildred said that some patients expressed such relief over removal of the stench that they thought their trip to the clinic was worthwhile even if no other benefits resulted.(16) Patients continue with this antiseptic wash at home once in the morning and at night.(18)

A yellow camphor salve was applied to certain superficial cancers and on the area where the dead tissue had dropped off after escharotic treatment. It softened the tissue so that the circulation could better reach it with the constituents of the internal tonic. The contents of the camphor salve were not revealed to me at the clinic.(16) A concentrated form of this ointment is given to patients to be mixed with equal parts of white Vaseline and spread on cotton as a dressing for lesions morning and night after washing.(18) The source of "additional Hoxsey formulas" describes a yellow salve made with Vaseline, lump rosin, refined camphor, refined beeswax, tincture of myrrh, and oil of spike.(15)

Mildred said the camphor salve would help to control and cure melanoma but that it took longer than when the red paste was used. Because it works quicker than the yellow, the red paste is usually used on melanomas. An 80% cure rate for melanoma was claimed. The red paste was also applied when the cancer was near the surface but under the skin. Ice packs are used for relief of pain. Pain from the action of the red paste was said to be so penetrating that it cannot even be blocked by injecting a local anesthetic. One melanoma patient reported that the pain began 20 minutes after it was applied. Burning pain continued for 5-7 days. The first 2 or 3 days were the worst, after which she was given non-narcotic pain medication. The reluctance to use narcotics is due to the susceptibility of individuals becoming addicted rather than to any interference the drugs may have with the tonic's actions.(16)

After visiting the Bio-Medical Center in Tijuana I concluded that no two external cancer cases were treated exactly the same. I observed 10 patients for only one clinic visit each, and their treatments varied greatly. Two other patients had three visits each, and two patients were treated five times in eight working days. A woman with a lesion extending from the sight of previous surgical excision of a basal cell carcinoma on the bridge of her nose had yellow ointment applied. It was observed the next day, and the following day the yellow salve was applied again to be left on for five days. Her return to the clinic was recommended to be in one year if all was well. A man with a squamous cell (?) carcinoma on his left shoulder had yellow powder directly applied which was covered by a thin layer of camphor salve on cotton (plain, not gauze) to be changed morning and night. In three days he returned and more camphor salve was applied on cotton. In two days more yellow powder was applied to the edges of the lesion, while red paste was applied to two spots in the center. This was covered with cotton and taped on; the dressing was to be removed in three days. Another woman had a regrowth of a melanoma where it had been previously excised. Yellow powder in a gel was place over the lesion and red paste on the incision scar. This was repeated in two days. Two days later the area was dressed. In another three days there was drainage around the eschar. Two days after this the necrotic tissue was still attached at its base but was expected to come off the next day.(16)

Therapeutic Adjuncts

Besides the internal tonic and the external escharotics, the Hoxsey treatment employs a number of additional features that help to improve response to these therapies and the ultimate outcome. Foremost among these features is the special diet that is followed. Unlike many other approaches, the main emphasis is on certain food substances to be avoided. These include pork, tomato, and vinegar and any products containing them. For instance, foods cooked in or containing lard are forbidden. The reason for their exclusion is due to the belief that these three food items somehow interfere with the effects of the tonic. This is based on years of empirical observation. Mildred stated that these foods can nullify the effects of the tonic for five days, and it can take up to three months to make up the lost ground. Other dietary restrictions that are emphasized include no alcohol, no salt, no white sugar or artificial sweeteners, no carbonated beverages, and no bleached flour products. Highly seasoned foods should be eliminated. Patients are encouraged to drink large amount of unsweetened grape juice mixed half with water. All types of fresh fruit juices are permitted. Patients must drink at least two quarts of fluids daily.(16,17,18)

Certain dietary supplements are covered by the treatment fee and supplied by the Bio-Medical Center. Yeast tablets are given as sources of vitamin B complex. A minimum of one gram daily of vitamin C is given, but it is recommended to be used to bowel tolerance or given intravenously when possible. The vitamin C is taken with 64 mg iron sulfate tablets after meals. Calcium with vitamin D is also taken after meals. High doses of calcium are used when there

is bone metastasis.(16,17,18) Other supplement recommendations include water-soluble vitamin A (beta-carotene) at no more than 25,000 IU per day, and vitamin E at not more than 100 IU per day.(16)

Other medications given at the Bio-Medical Center are an additional cost and depend on the patient. These include garlic, thymus gland extract, Probolin liver, superoxide dismutase, vitamin B12, Gerovital, D.M.S.O., Schulte's medications, and others. Syringes and needles are also sold.(16,18) Testosterone was sometimes used as an estrogen depressor or is given to alternate with tamoxifen for breast cancer patients already using the latter when they have become desensitized to it. At the time I visited diethylstilbesterol was given to some men with prostatic or testicular cancer. Sunscreen was emphasized as an important application for all patients with external cancers.(16)

BCG (bacillus Calmette-Guerin) subcutaneous injections were given in certain severe cancer cases, especially melanomas, to boost the immune response. The product used was manufactured in France and was claimed to be twice as potent as American-made brands. I observed only one BCG injection. Afterward the patient reported that the site hurt intensely. After two days it began to look like a boil. The injection site was expected to drain for 3-6 weeks and remain painful for three months. BCG was not used for lymphomas, since it increases their size. Instead, PPD (purified protein derivative) was given in lymphomas and in other less severe cases.(16)

If lab tests indicate syphilis or other infectious diseases, these are given the appropriate antibiotic.(1,18) When sulfa drugs are used the tonic is stopped until 24 hours after the last sulfa drug is taken. Antacids (Tri-tabs) or laxatives were prescribed when indicated.(18)

Medical treatments, techniques, and devices that cancer patients are warned to avoid include cortisone and any sort of heat applications. Mildred believes that these stimulate the growth of cancer. Implants, prostheses, biopsies, and surgery are dangerous in her mind because of the risk of inducing metastasis. Chemotherapy was said to destroy the body's immune defense and render the system more susceptible to the cancer. The tonic was believed to work best when patients have not received previous chemotherapy treatment or invasive surgery.(16)

DISCUSSION

The use of topical treatments in conjunction with the Hoxsey tonic speeds recovery by destroying the tumor mass without invasive surgical techniques that increase the risk of metastasis from detached cancer cells entering the circulation. The risks inherent in the topical treatment with escharotics require a firm knowledge of the underlying anatomy and clinical training concerning the frequency and type of application. The pain caused by the zinc chloride escharotic is a significant drawback, but a condition that patients seem willing to tolerate when confronted with the alternatives of surgery, radiation, or metastasis. In terms of efficacy with minimal suffering or damage to normal tissue, Mohs' chemosurgical technique appears to approach a happy median between escharotics and surgery for treating topical cancers.

The dietary and supplement regimen is holistically oriented. Besides avoiding those foods that interfere with the tonic, the rest of the prescribed diet avoids processed foods that have been depleted of trace nutrients. Additives and condiments that act as irritants (alcohol, spices) or upset biochemical equilibrium (table salt, sweeteners) help to optimize normal function. Supplements provide vitamin and mineral cofactors that are necessary for maintaining good health. In this area, modern naturopathic knowledge, practice, and products are more sophisticated than those used with the Hoxsey treatment. Enhancing the supplement prescription would be more a matter of degree than substance, however, and can (and should) be modified to meet individual patient needs.

When it comes to prescribing medication, the Hoxsey treatment utilizes both conventional medicines and other substances that would be considered experimental. Most naturopathic doctors are familiar with many of the experimental approaches mentioned, and many others exist that could be incorporated to advantage in particular cases. The primary criteria for adjunctive therapies are that they support normal biological processes and do not interfere with the action of the tonic. This allows for many approaches to be used in conjunction with the Hoxsey treatment. The unfortunate conflict comes into play when surgery, radiation therapy, or chemotherapy are utilized.

IV. PATIENT MANAGEMENT

Medical Care, Cost, and Follow-up at the Tijuana Clinic

At the time of my visit to the Bio-Medical Center in Tijuana in 1984 the medical staff was comprised of four Mexican medical doctors who spoke fluent English. The clinic was housed in a large mansion with an aviary in the courtyard, located on a hillside overlooking the city. Patients were requested to go without breakfast and to take a laxative the night before their visit. They arrived at the clinic without appointments early in the morning on a shuttle bus from an American border motel for a one-day visit. After they checked in, specimens were collected for urine and blood tests by laboratory technicians. Standard tests ordered included a UA, CBC with differential and ESR, a VDRL test for syphilis, alkaline phosphatase (and acid phosphatase for men), BUN, SGOT, and special tests were done when indicated. Next, a medical history and complete physical examination were performed by one of the doctors. On the several cases that I observed, these were both thorough. X-rays were then taken. Standard views included an AP and lateral of the chest, abdomen, and pelvis. Computerized tomography scans were available at the clinic when required. The clinic accepted recent laboratory reports and x-rays that patients brought with them. When x-ray and test results were available, the doctors met in general consultation together with Mildred Nelson and a medical doctor from a nearby hospital who specialized in radiology. During these consultations the diagnosis and therapeutic adjustments were discussed. Doctors then met again with the patients they had examined that day and discussed test results, diagnosis, and treatment. Instruction sheets were given to the patients and their questions were answered. There did not appear to me to be any rushing at any time throughout this process. Prescriptions given by the doctor were filled at the clinic pharmacy next door, the former site of the clinic. Patients requiring treatment for external cancerous lesions returned to the clinic as determined by Mildred Nelson. Mildred treated the external cases throughout the day and participated in exams and patient conferences when requested.(16,18)

It has been reported that currently all patients are tested for systemic yeast infection by *Candida albicans* before treatment begins, though the patient literature does not give the reasons for this test.(17) When I visited the the clinic, Mildred was very enthusiastic about a book she had read by Dr. William Crook entitled The Yeast Connection. This book documented the common flourishing of this yeast in individuals after long periods of using broad-spectrum antibiotics and/or after women taking birth control pills. The resulting

systemic infection was believed to cause a wide variety of symptoms and to impair the immune response. Reportedly, significant improvements in cancer patients in Australia with this condition occurred when nystatin was utilized to fight the yeast infection and vitamin C, a rotation diet, and avoidance of yeast-containing foods were employed to help control the condition.(16) I assume that if this protocol is now used at the Hoxsey clinic that it would include utilizing another source of vitamin B complex in place of yeast tablets.

The treatment, which included office calls, doctor's fees, and medications (tonic and vitamins) for as long as necessary, was a one-time charge of $2,000. A down payment of at least 30% was paid on the first visit. Additional fees for laboratory, x-ray, and physical examination charges ran between $150-$450. X-rays were $25 each and lab work varied in cost from $150-$175. CAT scans varied in cost from $325-$500. These were paid on the day of the examination. Other charges were made for auxiliary medications. Payment arrangements were made at the end of the visit, prior to obtaining any medication.(18,21) Mildred claimed that they never turn away patients in need due to lack of finances, but she required a letter from their banker or minister verifying the fact. She insisted that she had never sent a patient a bill for services rendered.(16)

Patients were not required to wait the predetermined time (usually 3-6 months) before returning to the clinic for reevaluation but were welcome to return at any time.(18) Follow-up in practice was the responsibility of the patient. No apparent attempt was made to maintain any contact through correspondence. Mildred believed that her results were slightly better than for Hoxsey with new additions incorporated into the regimen, but that cancers in general were getting worse and killing people faster. Based upon those patients that do remain in touch, Mildred believed that while many were not cured, all received some benefit from the Hoxsey treatment. She said their pain and suffering was reduced and their quality of life was improved.(16)

The limited follow-up study begun by Dr. Steve Austin in 1984 has recently been completed and published. The preliminary results were comparatively better with the Hoxsey treatment than for two other alternative approaches available at Tijuana clinics. A selection of 39 patients with a malignancy diagnosis reportedly confirmed by biopsy in American facilities were interviewed at the clinic from 1983 to 1984, but medical records for many were not available. Of these, 23 were lost to follow-up in the first four years, though eight of these had continued correspondence for nearly two years. Follow-up was done yearly by mail. Of the 16 remaining patients followed from 4-5 years or until death, nine had claimed to have advanced stages of cancer and 12 had previously been treated unsuccessfully with surgery, chemotherapy, and/or radiation combinations. Ten of the 16 died after an average survival time of 15.4 months. Seven of these had advanced cancer at the time of visiting the Bio-Medical Center. The average time of follow-up for the six survivors was 58 months. These patients included two cases of lung cancer (one advanced), two melanoma cases (one with level V), one recurrent bladder cancer patient, and one case of labial cancer.(95) No information was given to indicate whether the patients were questioned about compliance with the prescribed treatment or about any changes in their quality of life.

DISCUSSION

Both Harry Hoxsey and Mildred Nelson have attempted to maintain professional medical supervision over the treatment of cancer patients utilizing their remedies. This was often frustrated by legal entanglements and charges of quackery in connection with the treatment. Conventional medical protocols were not followed by those who practiced with Hoxsey.(96) However, the methods used were consistent with his theory of healing. While regular doctors required biopsies for diagnosis, Hoxsey believed after much clinical experience in observing the consequences that biopsies were dangerous and therefore inappropriate. While surgery and radiation therapy were mainstays in the orthodox treatment of cancer, Hoxsey was convinced that these spread the cancer and reduced the patient's natural ability to fight the disease. He was correct in asserting that radiation is a cause of malignancy, as daily news reports confirm. His escharotics could be painful and destructive but were effective means of eradicating some malignancies locally without dissemination.

As time progressed the protocol used by the Hoxseys and especially by Mildred Nelson adapted new features that both acknowledged technical advances in diagnostic assessment and practical developments in patient health care and support. The incorporation of supportive therapies that can potentially enhance outcome by working in concert with normal physiology has given the Hoxsey treatment an advantage over other treatments which rely exclusively on a herbal formula or some other single substance or method.

One aspect of the clinical environment that cannot be overemphasized is the sense of hope that is given the patient. In contrast to hospital cancer wards and centers that I have experienced, the prevailing attitude at the Bio-Medical Center was emotionally uplifting. The airy waiting room with light streaming through large windows was lively with talk, especially of patients who were returning after years or decades of treatment. This produced at times a cheerful atmosphere. Of course, the returning patients were for the most part the success stories, but listening to them relate their experience with the Hoxsey approach after undergoing unsuccessful attempts at cure through conventional means gave comfort to new patients. The possibility that the future may not be a downward spiral through growing pain and disability seemed to enliven many who harbored serious doubts. This may be disregarded by some as merely a short-lived placebo effect, but limiting the possibilities of its power to influence outcome may be one of the most serious mistakes made with ordinary prognosis. It is one thing for a doctor to admit that their technical knowledge and treatment have limitations that show no promise of cure for certain individuals who will need to look elsewhere if they intend to overcome their disease. It is quite another thing to instruct a seriously ill patient that there is no hope for cure and leave them condemned to die. This is placing human limitations on the healing power of nature and of God which have been proven time and again to be beyond the scope of our reasoning.

The lack of research and follow-up have been used by critics to discredit the results that Hoxsey and Mildred claim. Yet the funding that allows such laboratory and clinical research and follow-up to progress is entirely lacking for this approach. Add to this the fact that from its inception the treatment has not been refused to those who lack the means to pay, and that many are treated gratis while others make minimal payments for life-long treatment, it is a wonder that the income generated by the clinics has been adequate to maintain such modern facilities and professional staff as they have had. In the meantime billions of dollars have been poured into research that

has yielded few treatments of lasting benefit for many cases. The area of medicine where an arrogant attitude is most out of place is in the search for an effective treatment for cancers. This is a challenge that not only confronts the greatest medical minds but also every clinical practitioner and every family member who is faced with suffering that cannot at present be overcome.

V. CONCLUSIONS

There is much to be criticized and defended in the history of the Hoxsey treatment. One of the more disturbing aspects is the secrecy involving the formula for the tonic. The full revelation of the tonic and escharotic formulas, their variations, and clinical protocols is imperative. Mildred Nelson is reaching an age when the possibility of her sudden demise and the resulting loss of her unique knowledge and experiential insights becomes more likely. It appears at this point that no one has been trained to continue in her place. Mildred has expressed skepticism about the possibilities of the Hoxsey treatment ever being utilized in the United States given the legal harassment suffered by Harry Hoxsey. However, the days have arrived when doctors interested in clinical research could be attracted to participate in controlled studies with patients whose therapeutic options are limited or exhausted. These cases would involve many of the same types of patients that traditionally sought the Hoxsey treatment. Such cases could include types of cancers for which there is currently no conventional cure available, patients who have exhausted the conventional possibilities for effective cancer control, and those who refuse to submit themselves to the conventional therapeutic options currently available. The continual loss of lives to melanoma alone warrant clinical studies which include the tonic as part of the protocol. It is time to apply the attitude of hope to overcoming long-standing obstacles to the Hoxsey treatment.

This leads to another disturbing aspect of the Hoxsey saga. It involves refusal by the medical establishment to seriously consider studying the basic Hoxsey treatment on its own terms. Rather than trying to define cancer therapies as those means by which tumor cells are directly destroyed by the medicinal agent, medical innovators need to face the challenge of investigating means that can enhance the body's own methods of eradicating malignancies. This is not the first suggestion that the Hoxsey treatment needs to be examined by qualified medical investigators. Hoxsey's book details his struggle to persuade medical authorities to open an impartial investigation that he was incapable of managing himself. Politicians, patients, and writers have pleaded for further study. The most recent preliminary follow-up study gives further impetus and support to such research. The necessary arrangements were detailed by the University of British Columbia faculty committee at the beginning of their report on the Hoxsey treatment which was limited by personnel, time, and funding. "The ideal in cancer investigation would be a long-range study occupying the time and effort of a number of professionally trained persons over a period of five to ten years. Such as investigation would involve the close study of a large number of cases, with adequate controls, together with the necessary laboratory and statistical investigation, in an attempt to arrive at a sound evaluation of the claims that have been made. A great deal of planning would also be required, and suitably trained personnel would have to be recruited. Large sums of money would be necessary."(96)

The needs have been identified. What is required is a sufficient response.

1. Bernard, A. A cure for cancer? Man's Magazine Aug., 1953 (reprinted in Prevention pp. 19-33, Oct., 1953)
2. Bureau of Investigation. Mr. Hoxsey has a setback. J..A.M.A. 150(1):54-55, 1952
3. Bur. Invest. The Hoxide cancer "cure." J.A.M.A. 86(1):55-7, 1926
4. Bur. Invest. Comment on court opinion that internal cancer can be cured with medicine. J.A.M.A. 145(4):252-3, 1951
5. Bur. Invest. Cough medicine for cancer? J.A.M.A. 155(7):667-8, 1954
6. Comm. on Nat. Form., National Formulary, 5th ed., Am. Pharm. Assoc., Washington, D.C., 1926
7. Comm. on Nat. Form., National Formulary, 6th ed., Am. Pharm. Assoc., Washington, D.C., 1935
8. Davis GS. Organic Materia Medica, 2nd ed., Parke, Davis & Co., Detroit, Mich., 1890
9. anon. Favorites for many years. Parke, Davis & Co. advertisement, circa 1900
10. Felter HW, Lloyd JU. King's American Dispensatory, 18th ed., 3rd rev., 1898, reprinted by Eclectic Medical Pub., Portland, Ore., 1983
11. Hartwell JL. Plant remedies for cancer. Canc. Chemother. Rep. 7:19-24, 1960
12. Lloyd JU. History and names of Rhamnus purshiana (cascara sagrada). Am. Jour. Pharm. pp. 467-9, Sep., 1896
13. Grieve M. A Modern Herbal, Harcourt, Brace & Co., 1931, reprinted by Dover Pub., Inc., New York, 1971
14. Larrick GP. The Hoxsey cancer "cure." Consumer Rep. 21:303, 1956
15. Brown AJ. March of Truth on Cancer, Arlin J. Brown Information Center, Fort Belvoir, Virg., n.d.
16. Brinker FJ. Notes on Hoxsey treatment from visit to Bio-Medical Center, Tijuana, Mex., Jan. 30-Feb. 8, 1984
17. Office of Technology Assessment. Unconventional Cancer Treatments, Chap. 4, "Herbal Treatments," pp. 69-87, Congress of the United States, Washington, D.C., 1990
18. anon. Loose-leaf patient handouts. Bio-Medical Center, Tijuana, Mex., obtained at the clinic in 1984
19. Jones E. Definite Medication, 1910, reprinted by Jain Publishing Co., New Delhi, India, n.d.
20. Hartwell JL. Plants Used against Cancer, A Survey, Quarterman, Pub., Lawrence, Mass., 1982
21. anon. Do You Have Cancer? Patient pamphlet from Bio-Medical Center, Tijuana, Mex., n.d.
22. Felter HW. The Eclectic Materia Medica, Pharmacology and Therapeutics. John K. Scudder, Cincinnati, Ohio, 1922
23. Brinker FJ. Formulas For Healthful Living, Eclectic Medical Pub., Sandy, Ore., in press
24. Belkin M, Hardy WG, Perrault A, Sato H. Swelling and vacuolization induced in ascites tumor cells by polysaccharides from higher plants. Cancer Res. 19:1050-62, 1959
25. Guggolz J, Livingston AL, Bickoff EM. Detection daidzein, formononetin, genistein, and biochanin A in forages. Agric. Fd. Chem. 9(4):330-2, 1961
26. Dedio W. Variation in estrogenic-like substances in red clover and alfalfa as related to environment, varieties and stage of growth. Diss. Abs. Int. B 34(11):5281-2, 1974
27. Bickoff EM, Livingston AL, Hendrickson AP, Booth AN. Relative potencies of several estrogen-like compounds found in forages. Agric. Fd. Chem. 10(5):410-2, 1962
28. Martin PM, Horwitz KB, Ryan DS, McGuire WL. Phytoestrogen interaction with estrogen receptors in human breast cancer cells. Endocrinol. 103(5):1860-7, 1978
29. Shutt DA. The effects of plant oestrogens on animal reproduction. Endeavor 35:110-3, 1976
30. Cheng E, Story CD, Yoder L, Hale WH, Burroughs W. Estrogenic activity of isoflavone derivatives extracted and prepared from soybean oil meal. Science 118:164-5, 1953

31. Boyle W. Official Herbs - Botanical Substances in the United States Pharmacopoeias 1820-1990, Buckeye Naturopathic Press, East Palestine, Ohio, 1991
32. Gibson MR. Glycyrrhiza in old and new perspectives. Lloydia 41(4):349-54, 1978
33. Doll R, Hill ID, Hutton C, Underwood KJ II. Clinical trial of a triterpenoid liquorice compound in gastric and duodenal ulcer. Lancet pp. 793-6, Oct. 20, 1962
34. Tangri KK, Seth PK, Parmar SS, Bhargava KP. Biochemical study of anti-inflammatory and anti-arthritic properties of glycyrrhetic acid. Biochem. Pharmacol. 14:1277-81, 1965
35. Tamura Y, Nishikawa T, Yamada K, Yamamoto M, Kumagai A. Effects of glycyrrhetinic acid and its derivatives on D4-5a- and 5b-reductase in rat liver. Arzneim.-Forsch. 29:647-9, 1979
36. Bannister B, Ginsburg R, Shneerson J. Cardiac arrest due to liquorice-induced hypokalaemia. Br. Med. Jour. Sep. 17, 1977
37. Wash LK, Bernard JD. Licorice-induced pseudoaldosteronism. Am. J. Hosp. Pharm. 32(1):73-4, 1975
38. Abe N, Ebina T, Ishida N. Interferon induction by glycyrrhizin and glycyrrhetinic acid in mice. Microbiol. Immunol. 26(6):535-9, 1982
39. Nishino H, Kitagawa K, Iwashima A. Antitumor-promoting activity of glycyrrhetic acid in mouse skin tumor formation induced by 7,12-dimethylbenz[a]anthracene. Carcinogen. 5(11):1529-30, 1984
40. Kitagawa K, Nishino H, Iwashima A. Inhibition of the specific binding of 12-O-tetradeconoylphorbol-13-acetate to mouse epidermal membrane fractions by glycyrrhetic acid. Oncology 43:127-30, 1986
41. Kumagai A, Nishino K, Shimomura A, Kin T, Yamamura Y. Effect of glycyrrhizin on estrogen action. Endocrinol. Japon. 14(1):344-8, 1967
42. Reiners W. 7-Hydroxy-4'-methoxy-isoflavon (formononetin) aus sussholzwurzel. Uber inhaltsstoffe der sussholzwurzel. II. Experientia 22:359, 1966
43. Taylor A, KcKenna GF, Burlage HM. Anticancer activity of plant extracts. Tex. Rep. Biol. Med. 14:538-56, 1956
44. Vincent D, Segonzac G. Higher plants having antibiotic properties. Toulouse med. 49:669, 1948 (C.A. 44:10046i)
45. Schulte KE, Rucker G, Boehme R. Polyacetylenes as compounds of the roots of bur. Arzneim.-Forsch. 17(7):829-33, 1967
46. Reisch J, Spitzner W, Schulte K. The problem of the microbiological activity of simple acetylene compounds. Arzneim.-Forsch. 17:816-25, 1967
47. Morita K, Kada T, Namiki M. A desmutagenic factor isolated from burdock (Arctium lappa Linne). Mutation Res. 129:25-31, 1984
48. Morita K, Nishijima Y, Kada T. Chemical nature of a desmutagenic factor from burdock (Arctium lappa Linne). Agric. Biol. Chem. 49(4):925-32, 1985
49. Dombradi Ca, Foldeak S. Screening report on the antitumor activity of purified Arctium lappa extracts. Tumori, 52:173-6, 1966
50. Foldeak S, Dombradi GA. Tumor-growth inhibiting substances of plant origin. I. Isolation of the active principle of Arctium lappa. Acta Univ. Szeged., Acta Phys. Chem. 10:91-3, 1964 (C.A. 62:6339c)
51. Wolf S, Mack M. Experimental study of the action of bitters on the stomach of a fistulous human subject. Drug Standards 24(3):98-101, 1956
52. Ikram M. A review on the chemical and pharmacological aspects of genus Berberis. Planta Med. 28:353-8, 1975
53. Suess TR, Stermitz FR. Alkaloids of Mahonia repens with a brief review of previous work in the genus Mahonia. J. Nat. Prod. 44:680-7, 1981
54. Velluda CC, Goina T, Ticsa I, Petcu P, Pop S, Csutak W. Effect of Berberis vulgaris extract and of the berberine, berbamine, and oxyacanthine alkaloids on liver and bile function. Lucr. prez. conf. natl. farm., Bucharest pp. 351-4, 1958 (C.A. 53:15345a)
55. Turova AD, Konovalov MN, Leskov AI. Berberine, an effective cholagogue. Med. Prom. SSSR 18(6):59-60, 1964 (C.A. 61:15242f)
56. Amin AH, Subbaiah TV, Abrasi KM. Berberine sulfate: antimicrobial activity, bioassay, and mode of action. Can. J. Microbiol. 15:1067-76, 1969
57. Kumazawa Y, Itagaki A, Fukumoto M, Fujisawa H, Nishimura C. Activation of peritoneal macrophages by berberine-type alkaloids in terms of induction of cytostatic activity. Int. J. Immunopharmac. 6(6):587-92, 1984
58. Schmitz H. The influence of berberine on cellular metabolism. Z. Krebsforsch. 57:137-41, 1950 (C.A. 46:4680i)
59. Shvarev IF, Tsetlin AL. Antiblastic properties of berberine and its derivatives. Mater. Vses. Konf. Issled. Lek. Rast. Perspekt. Ikh Ispol'z. Proizvod. Lek. Prep. p. 245, 1972 (C.A. 83:674m)
60. Jones EG. Cancer - Its Causes, Symptoms and Treatment, Therapeutic Pub. Co., Inc., Boston, 1911
61. Stout GH, Malofsky, Stout VF. Phytolaccagenin: a light atom X-ray structure proof using chemical information. J. Am. Chem. Soc. 86:957-8, 1964
62. Waxdal MJ. Isolation, characterization, and biological activities of five mitogens from pokeweed. Biochem. 13(18):3671-7, 1974
63. Yokoyama K, Yano O, Terao T, Osawa T. Purification and biological activities of pokeweed (Phytolacca americana) mitogens. Biochim. Biophys. Acta 427:443-52, 1976
64. Reinherz EL, Kung PC, Goldstein G, Schlossman SF. Further characterization of the human inducer T cell subset defined by monoclonal antibody. J. Immunol. 123(6):2894-6, 1979
65. Barker BE, Farnes P, LaMarche PH. Peripheral blood plasmacytosis following systemic exposure to Phytolacca americana (pokeweed). Pediatrics 38(3):490-3, 1966
66. Youngken HW, Vander Wyk RW. Studies of National Formulary drugs. J. Am. Pharm. Assoc. 28:17-31, 1939
67. Adolf W, Hecker E. New irritant diterpene-esters from roots of Stillingia sylvatica L. (Euphorbiaceae). Tetrahed. Lett. 21:2887-90, 1980
68. McKenna GF, Taylor A. Screening plant extracts for anticancer activity. Tex. Rep. Biol. Med. 20:214-20, 1962
69. Crombie L. Amides of vegetable origin. Part III. Structure and stereochemistry of neoherculin. J. Chem. Soc. pp. 995-8, 1955
70. Rao KV, Davies R. The ichthyotoxic principles of Zanthoxylum clava-herculis. J. Nat. Prod. 49(2):340-2, 1986
71. Jacobson M. The structure of echinacein, the insecticidal component of American coneflower roots. J. Organic Chem. 32:1646-7, 1967
72. Fish F, Waterman PG. Alkaloids in the bark of Zanthoxylum clava-herculis. J. Pharm. Pharmac. 25 (Suppl.):115P-6P, 1973
73. Fish F, Gray AI, Waterman PG, Donachie F. Alkaloids and coumarins from North American Zanthoxylum species. Lloydia 38:268-70, 1975
74. Cordell GA, Farnsworth NR. Experimental antitumor agents from plants, 1974-76. Lloydia 40(1):1-44, 1977
75. Stermitz FR, Larson KA, Kim DK. Some structural relationships among cytotoxic and antitumor benzophenanthridine alkaloid derivatives. J. Med. Chem. 16(8):939-40, 1973
76. Fairbairn JW. The active constituents of the vegetable purgatives containing anthracene derivatives. J. Pharm. Pharmacol. 1:683-92, 1949
77. Hoerhammer L, Wagner H, Hoerhammer HP. New methods in pharmacognostical education. XIII. Thin-layer chromatography of components of Rhamnus cortical drugs and their preparation. Deut. Apoth.-Ztg. 107(17):563-6, 1967 (C.A. 67:84920u)
78. Mary NY, Christensen BV, Beal JL. A paper chromatographic study of aloe, aloin and of cascara sagrada. J. Am. Pharm. Assoc. 45:229-32, 1956
79. Lish PM, Dungan KW. Peristaltic-stimulating and fecal-hydrating properties of dioctyl sodium sulfosuccinate, danthron, and cascara extracts in the mouse and rat. J. Am. Pharm. Assoc. 47:371-5, 1958

80. Tyson RM, Shrader EA, Perlman HH. Drugs transmitted through breast milk. J. Pediatr. 11:824-32, 1937
81. Dwivedi SPD, Pandey VB, Shah AH, Rao YB. Chemical constituents of Rhamnus procumbens and pharmacological actions of emodin. Phytother. Res. 2(1):51-3, 1988
82. Kupchan SM, Karim A. Tumor inhibitors. 114. Aloe emodin: antileukemic principle isolated from Rhamnus franguls L. Lloydia 39(4):223-4, 1976
83. Ruggieri R. Application of the potentiometric method in a water-free medium for the determination of anthraquinone derivatives in drugs. Boll. chim. farm. 96:491-4, 1957 (C.A. 55:5874e)
84. Tin-Wa M, Fong HHS, Abraham DJ, Trojanek J, Farnsworth NR. Structure of sanguidimerine, a new major alkaloid from Sanguinaria canadensis (Papaveraceae). J. Pharm. Sci. 61(11):1846-7, 1972
85. Tin-Wa M, Farnsworth NR, Fong HHS, Trojanek. Biological and phytochemical evaluation of plants. VIII. Isolation of a new alkaloid from Sanguinaria canadensis. Lloydia 33(2):267-9, 1970
86. Mitscher LA, Park YH, Clark D, Clark GW III. Antimicrobial agents from higher plants. An investigation of Hunnemannia fumariaefolia pseudoalcoholates of sanguinarine and chelerythrine. Lloydia 41:145-9, 1978
87. Vichkanova SA, Rubinchik MA, Adgina VV, Fedorchenko TS. Chemotherapeutic action of sanguinarine. Farmakol. Toksikol. (Moscow) 32:325-8, 1969 (C.A. 71:59405e)
88. McDonald J. Physiologic Medication, Armstrong Pub., Chicago, Ill.; 1900
89. Nichols P. The Value of Escharotic Medicines, Dr. Nichols Sanatorium, Savannah, Missouri, 1949
90. Mohs FE. Chemosurgery - a microscopically controlled method of cancer excision. Arch. Surg. 42:279-95, 1941
91. Mohs FE. Chemosurgical treatment of cancer of the skin. J.A.M.A. 138(8):564-9, 1948
92. Phelan JT, Milgrom H, Stoll H, Traenkle. The use of Mohs' chemosurgery technique in the management of superficial cancers. Surg. Gyn. Obs. pp. 25-30, Jan. 1962
93. Mohs FE. Chemosurgery for facial neoplasms. Arch. Otolaryng. 95:62-7, 1972
94. Jordan RT, Allen LM. Drugs for the treatment of skin disorders and tumors containing catecholic butanes and zinc compounds. Chem. Abs. 110:415(#179544v), 1989
95. Austin S, Dale EB, DeKadt S. Long term follow-up of cancer patients using Contreras, Hoxsey and Gerson therapies. J. Naturop. Med. 5(1):75-6, 1994-5
96. Mather JM (Comm. Chair.) et al. Report of a Committee of Faculty Members of the University of British Columbia concering the Hoxsey Treatment for Cancer, University of British Columbia, Vancouver, Can., 1957

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Review article

Alternative pharmacological and biological treatments for cancer: Ten promising approaches

Ralph W. Moss, Ph.D.

There are well over 100 promising alternative treatments for cancer (1). How can clinicians and patients choose the best therapies? How can scientists know which methods are most promising to research? Clearly, one would like to base decisions on scientifically credible studies of such methods. But for a variety of reasons such tests have rarely been performed.

One major problem has been the difficulty of conducting clinical trials that will pass muster with a skeptical (if not downright hostile) Food and Drug Administration (FDA). The cost of such new drug development has been estimated at over $125 million per item, with a development time of up to ten years *(New York Times,* Feb. 9, 1988).

Such expenditures are tolerable for giant pharmaceutical companies, with their huge research and development budgets. In fact, the high regulatory barrier may actually benefit the largest companies. "These regulations favor companies with greater financial strength," said one spokesperson for the smaller drug companies. "They're eliminating competition" *(Business Week,* Jan. 17, 1977). The key point is that the most promising alternative approaches are found in the public domain, as either inexpensive natural substances or common chemical agents. They generally cannot be strongly patented. This means that the major pharmaceutical companies, who are always a major factor in the direction of cancer research, are rarely interested in investing the enormous sums required for full trials.

Developers of alternative methods often find themselves barred from interstate commerce under Title 21, article 355 of the U.S. Code, which states that unless a developer has presented "substantial evidence" of a drug's safety and efficacy, the FDA can deny approval for marketing. And this has in fact been the case with most alternative drugs and vaccines for cancer. Therefore, it is not surprising that many such products fail to obtain FDA approval for marketing and wind up in a kind of gray market, the "cancer underground."

Such difficulties have gone hand-in-hand with a long-standing prejudice of the dominant medical establishment. According to this prevalent view, alternative treatments for cancer should not even exist; they are an expression of "health fraud" or "quackery." Self-described "quackbusters," centered in aggressive groups such as the American Cancer Society's "Questionable Methods" subcommittee and the National Council Against Health Fraud (NCAHF), have expended considerable energy to convince the medical profession and the general public that alternative cancer treatments are automatically suspect. In some states, such as California, alternatives to surgery, radiation, and toxic chemotherapy are actually outlawed by statute.