# Unconventional therapies for cancer: 1. Essiac

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*Education*

*Éducation*

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The Canadian Breast Cancer Research Initiative does not endorse the use of any particular unconventional therapy. It urges patients to evaluate all evidence carefully and to consult their caregiver in order to make thoughtful and fully informed personal decisions.

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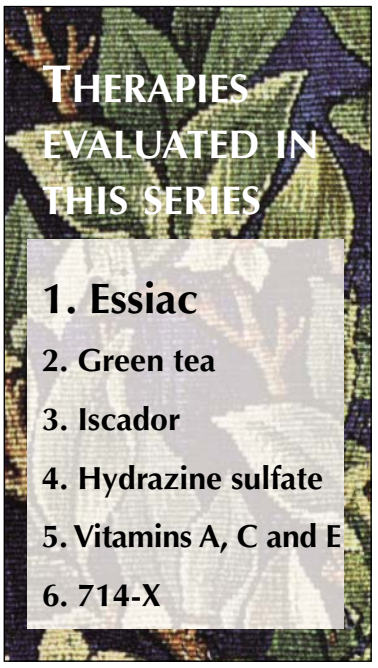
## Abstract

PHYSICIANS AND PATIENTS HAVE BEEN FRUSTRATED by the lack of reliable information on unconventional therapies. To help fill this gap in the area of breast cancer therapy, the Canadian Breast Cancer Research Initiative formed a task force to advise it on how best to promote research into unconventional therapies. As part of the work of the task force, a review of the available literature was carried out for each of the following products: Essiac, green tea, Iscador, hydrazine sulfate, vitamins A, C and E, and 714-X. The first article in this series on unconventional therapies for cancer describes the methodology used to obtain and evaluate the information and provides a summary of the findings on Essiac. Subsequent articles will cover the other products. For most of the products reviewed, there has been some indication of possible benefit but no definitive evidence. Innovative and collaborative research needed to meet the information needs of growing numbers of patients and their physicians is now being sponsored by the Canadian Breast Cancer Research Initiative. Open communication between patients and physicians is also necessary for the maintenance of an appropriate therapeutic partnership and for the identification and control of side effects. The Ontario Division of the Canadian Cancer Society, a partner in the Canadian Breast Cancer Research Initiative, supported the preparation of a patient-information piece on unconventional therapies to accompany the series. This item will assist patients who are considering such therapies and will promote open communication between patients and their physicians.

## Résumé

LE MANQUE D'INFORMATION FIABLE sur les thérapies non conventionnelles est cause de frustration pour les médecins et les patients. Afin d'aider à combler cette lacune dans le domaine du traitement du cancer du sein, l'Initiative canadienne de recherche sur le cancer du sein a créé un groupe de travail chargé de la conseiller sur les meilleures façons de favoriser la recherche sur les thérapies non conventionnelles. Le groupe de travail a notamment étudié la littérature disponible sur les produits suivants : Essiac, thé vert, Iscador, sulfate d'hydrazine, vitamines A, C et E, et 714-X. Dans le premier article de cette série sur les thérapies non conventionnelles du cancer, les auteurs décrivent la méthodologie utilisée pour réunir et évaluer l'information et résument les constatations sur l'Essiac. D'autres articles à venir porteront sur les autres produits. Pour la plupart des produits étudiés, on a constaté des avantages possibles, mais on n'a établi aucune preuve concluante. L'Initiative canadienne de recherche sur le cancer du sein parraine maintenant des recherches collaboratives novatrices nécessaires pour répondre aux besoins d'information des patientes de plus en plus nombreuses et de leurs médecins. La communication ouverte entre les patients et les médecins est aussi nécessaire au maintien d'une alliance thérapeutique appropriée et à l'identification et au contrôle des effets secondaires. Le chapitre ontarien de la Société canadienne du cancer, partenaire de l'Initiative canadienne de recherche sur le cancer du sein, a appuyé la préparation d'un document d'information destiné aux patients sur les thérapies non conventionnelles pour accompagner la série. Ce document aidera les patients qui envisagent de suivre de telles thérapies et préconisera la communication ouverte entre eux et leurs médecins.



The use of unconventional therapies has increased dramatically over the past 5 to 10 years. Recent surveys have shown that unconventional therapies are used by 40% to 60% of the population and are of particular interest to people with some higher education, women and people with chronic diseases such as cancer.[1,2]

Physicians are often uncomfortable when their patients indicate an interest in unconventional therapies and ask for advice. Unlike conventional therapies, which are usually only made available after formal scientific study of their safety and effectiveness, unconventional therapies are often released to the public without any scientific evaluation. Furthermore, although information about the effects of conventional therapies is readily available to physicians, information on unconventional therapies is difficult to obtain, leaving physicians with few data on which to base their advice. Although many conventional therapies are known to be based on "natural products" and many established therapies have not undergone the level of rigorous evaluation now demanded of new therapeutic approaches, physicians are particularly sceptical about unconventional therapies.

Open communication between patients and physicians is critical to the maintenance of an appropriate therapeutic partnership and to the proper identification and control of untoward or unexpected effects. Open communication is also important when patients are using or are considering using unconventional therapies; however, such communication is often hampered by patients' perceptions that physicians know little about these therapies or their perceptions that they will be ridiculed for considering them. Thus, physicians will often need to initiate and maintain open communication to assist their patients in making informed and safe decisions about the use of unconventional therapies. [A patient-information piece written for people who are considering unconventional therapies in general will be published later in the series. It will provide patients with advice on sources for information, cautions regarding the interpretation of available information and a strong recommendation to maintain open communication with their physicians.]

In this series, the term "unconventional" is used to include a broad range of therapies that are not taught in medical schools and not usually recommended or provided by physicians. There is currently much discussion over the terminology. However, the task force chose this term because it is not pejorative in the sense that "unproven" is, and it includes therapies that patients use along with conventional therapies (complementary) and therapies that people use instead of conventional therapies (alternative).

Anyone who has sought information on unconventional therapies knows that there are very large gaps in our understanding of these therapies, even when data from international sources are considered. There is an urgent need for high-quality research to examine the safety and effectiveness of unconventional therapies, particularly those that are widely used and those for which there is currently some evidence of effectiveness.

In 1993, following the National Forum on Breast Cancer, the Canadian Breast Cancer Research Initiative (CBCRI) aligned its strategic planning with many of the recommendations made at the forum. Because participants expressed a need for increased research into the safety and effectiveness of unconventional therapies, the CBCRI established the Task Force on Alternative Therapies to determine how best to facilitate research in this area.

In order to make a preliminary assessment of the type, quality and sources of information currently available on the safety and effectiveness of unconventional therapies for cancer, the task force decided to assess the information available on a sample of 6 therapies known to be used by Canadian cancer patients. It soon realized that it could not conduct a formal review of the evidence such as one might do for a conventional therapy. The scientific data were limited, and even research studies reported in scientific journals were often characterized by incomplete data and poor study design. It was thought that this situation may have arisen because unconventional therapy providers and researchers are rarely affiliated with academic institutions and do not have access to research funds or to experts in research design, analysis and reporting. In addition, some providers and manufacturers may be resistant to participating in research studies, since negative results might adversely affect popularity and profits.

Because formal literature reviews were not possible, the task force decided to focus its efforts on preparing annotated bibliographies on the following unconventional therapies: Essiac, green tea, Iscador, hydrazine sulfate, vitamins A, C and E, and 714-X. It was hoped that the bibliographies would serve the dual roles of facilitating further research and providing summaries of existing information for the public.

## Accessing and assessing the information on unconventional therapies

Locating, obtaining and evaluating the literature on the chosen unconventional therapies presented a major challenge. A listing of publications relevant to these therapies cannot be readily obtained using computerized databases such as MEDLINE, Cancerlit and Toxline, and

many useful articles on unconventional therapies appear in the lay literature, magazines and books. Furthermore, because many unconventional therapies have been developed in Europe or Asia, articles describing their use and research into their effects are often available only in foreign-language journals or journals held only in specialty libraries.

Standard search processes using computerized databases identified only a small proportion of the published material that was ultimately found on the unconventional therapies selected for this review. A multimodal search process was developed to supplement traditional search techniques, with a system of tracking references from textbooks, magazine articles, proponents, manufacturers, the World Wide Web, unconventional care providers, health food stores, public libraries, regulatory bodies, national and international cancer organizations and their information services, other institutions known to be interested in the investigation of unconventional therapies, and personal contact with the authors of key articles. The searches were highly iterative and continued until few new items were being uncovered. Although several of the agents reviewed have been proposed for both the treatment and the prevention of cancer, the reviews emphasized evidence related to their possible value as treatments for cancer. The reviews were expanded to include evidence pertaining to the constituents of the agent where appropriate. Historical as well as current information was sought covering the period up to mid-1995.

Each item obtained was reviewed and classified as being "not very useful," "useful" or "very useful" depending on an assessment of the value of the reported results or the probable utility of the research methodology used. In some cases the assessment also considered the value of the references provided.

Although the process of assembling the information was careful and time-consuming, the task force recognized that some potentially useful information may have been unavoidably missed. As well, the review process was complicated by the need for reviewers to acquire an understanding of a wide range of disciplines including botany, biochemistry, animal research and clinical trials. Fortunately, the recent widespread interest in unconventional therapies has prompted the publication of new reference books, scientific journals and Web sources, making the collection and assessment of information on unconventional therapies a little easier. In addition, an informal network of researchers is being formed, and bibliographies and research experience are being shared. The developments will facilitate future research in this field.

The annotated bibliographies that were prepared by the task force are available in hard copy to researchers, health care providers and patients from the CBCRI (address appears at the end of the article). More detailed references for the information summarized in this article on Essiac, and in subsequent articles in the series, can be found in these annotated bibliographies. The bibliographic lists and the lay summaries (published in 1997) can be found on the CBCRI's Web site (**www.breast.cancer.ca**).

The following summary of the information found on Essiac expands the lay summaries for clinicians and provides references for the key findings. Subsequent articles in the series will summarize the findings on each of the other 5 therapies reviewed. [Copies of this and other articles in the series will be available on *CMAJ*'s Web site (**www.cma.ca/cmaj/series/therapy.htm**).]

## Essiac

### *What is it?*

Essiac is an herbal mixture that has been widely used in Canada for more than 70 years. The original recipe contained 4 herbs and is said to have been formulated by an Ojibwa healer "to purify the body and put it back in balance with the great spirit." In the 1920s Essiac was popularized by Rene Caisse, a nurse working in Bracebridge, Ont., who reported that she obtained the recipe from a woman claiming it had cured her breast cancer. The herbal mixture became known as Essiac (Caisse spelled backward).

The 4 main herbs in Essiac are burdock root (*Arctium lappa*), Indian rhubarb (*Rheum palmatum*), sheep sorrel (*Rumex acetosella*) and the inner bark of slippery elm (*Ulmus fulva* or *U. rubra*). Proponents of Essiac claim that it strengthens the immune system, improves appetite, relieves pain and improves overall quality of life. They also claim that it may reduce tumour size and prolong the lives of people with many types of cancer.

For 40 years Rene Caisse gave Essiac to several hundreds of cancer patients. She reportedly administered one of the herbs by injection and the others as a tea and modified the formulas several times on the basis of her experience. By 1938, concerns and questions about the use of Essiac led to an investigation by the Cancer Commission, established under the Cancer Remedies Act of Ontario (1938). Commission members visited the clinic where Caisse worked, heard testimonials from patients she had treated, expressed concern about her unwillingness to provide the formula to them for further analysis and concluded there was limited evidence for the effectiveness of Essiac. [The Cancer Commission submitted reports on various cancer remedies in addition to Essiac. Their re-

ports are held in Record Group 10, Series 106, at the Archives of Ontario, Toronto.] Nonetheless, her clinic continued to operate with public support, although without official approval.

Between 1959 and 1978 Caisse worked in partnership with a prominent American physician, Dr. Charles Brusch, to modify the recipe and promote its use. As a result of their clinical and laboratory work, they added 4 herbs to the original recipe — watercress, blessed thistle, red clover and kelp — which they believed potentiated its action and improved its taste. More important, the new mixture did not require injection and could therefore be used at home.

In 1977, a year before her death, Caisse gave one of her formulas for Essiac containing the 4 main herbs to Resperin, a Toronto-based corporation, in the belief that it would be tested and made available at a reasonable cost. In 1978 the Department of National Health and Welfare gave permission to Resperin to conduct studies of the safety and effectiveness of Essiac, but it withdrew its permission in 1982 after it became clear that the research was not proceeding as planned. Restrictions were placed on the promotion of Essiac for use in the treatment of cancer. The formula is now manufactured as Essiac® by Essiac Products in New Brunswick and is available in health food stores, from the manufacturer or through Health Canada's emergency drug release program on compassionate grounds. Another Canadian product — Flor-Essence® — believed to be the 8-herb recipe developed by Caisse and Brusch, is manufactured in British Columbia and is widely available in health food stores. The proponents and manufacturers of Flor-Essence® are careful not to make claims that it is useful as a cancer therapy; they promote it as a health-enhancing herbal tea.

The manufacturers provide instructions for preparing and storing Essiac. The tea is usually taken 1–3 times a day, on an empty stomach to minimize possible side effects of nausea, vomiting and diarrhea.

Proponents advise that Essiac is compatible with all other cancer treatments, including chemotherapy and radiotherapy. Most people trying Essiac today use it in addition to conventional treatments or as a component of care for terminal disease.

## Safety

Adverse effects associated with the use of Essiac have not been reported. However, the constituent herbs may cause allergic dermatitis in addition to their laxative effect. Also, burdock root has been linked to possible atropine-like toxic effects, but this may have been due to contamination.[3]

## Laboratory and clinical evidence

The search process did not identify any published reports of laboratory or clinical studies examining the effectiveness of Essiac, although a few unpublished papers and letters relating to both laboratory and clinical studies were found. Most of these concerned work conducted by Caisse and Brusch or to studies done on their behalf. However, the reports were incomplete and difficult to interpret.

At the request of Caisse and Brusch, researchers at the Memorial Sloan Kettering Laboratories, New York, conducted studies using Essiac in 1959 and from 1973 to 1976. Unfortunately, the researchers encountered difficulties with their test systems and were unable to establish the collaboration necessary to ensure that the preparation, administration and storage of the herbs were appropriate. Although preliminary reports suggested some evidence of biological activity, no conclusions were reached and the work was not publicly reported (unpublished statement by Brusch entitled "Essiac" held by the CBCRI, as well as unpublished letters and laboratory reports from Dr. C. Chester Stock, Memorial Sloan Kettering Cancer Center).

Another laboratory study conducted for Brusch revealed that, among mice injected with human cancer cells, those given oral and intravenous Essiac showed more tumour necrosis and cell degradation than control mice.[4]

Among the materials obtained for this review, there were many anecdotal and testimonial reports describing positive outcomes associated with the use of Essiac, some of which appeared remarkable and some of which were corroborated by physicians. However, information regarding the pathological diagnosis, stage of disease, conventional and unconventional treatments provided, and outcomes other than death was rarely provided in these reports, which made comparison with expected outcomes or the results of conventional treatments impossible.

A few studies involving groups of patients treated with Essiac were found, but it was unclear whether these were complete series, and thus it was difficult to know what proportion of patients taking Essiac might be expected to benefit.[5–7] An unpublished Canadian study of the effectiveness of orally administered Essiac, conducted in the 1970s, revealed no clinical benefit in terms of survival or tumour regression but some subjective improvements in symptom control and well-being (Dr. David Walde, Algoma District Medical Group, Sault Ste. Marie, Ont.: personal communications, 1995 and 1996). Although the Essiac used in the study had been obtained from Rene Caisse, a potential loss of potency of the stored product and the route of administration may have affected the results. The investigators were

also unable to persuade Caisse to allow them to develop a rigorous research design.

In the early 1980s the Department of National Health and Welfare reviewed the data derived from physicians supervising the care of 87 patients given Essiac on compassionate grounds between 1978 and 1982.[6] The data were incomplete, and no clear evidence of improved survival was reported. Other outcomes such as pain control and quality of life were not examined. Because there was no evidence of harm, the Department of National Health and Welfare continued to permit the use of Essiac on compassionate grounds.

No reports were found of case–control studies or randomized controlled clinical trials demonstrating that any observed positive outcomes in cancer patients can be attributed to Essiac rather than to other therapies or the natural course of the disease.

### Constituent herbs

Although Brusch advised that the herbs in Essiac had to be used in combination and in the correct proportions in order to be effective,[8] the available literature on each of the 4 main herbs and their constituents were reviewed.

A number of laboratory studies of burdock root and Indian rhubarb were found. Both of these herbs have a long history of use as folk medicines and are included in many compendia of herbal remedies,[9,10] being valued for their properties as laxatives, promoters of wound healing and folk remedies for cancer. They contain relatively high concentrations of flavones, anthraquinones, tannins and certain polysaccharides, which have been variously reported to have antioxidant, immunomodulatory, antimutagenic and cytostatic effects.[11–14] Interestingly, a number of conventional chemotherapeutic agents (e.g., adriamycin) are anthraquinone derivatives.[15] Burdock extract caused necrosis in solid tumours in mice[16] and has been found to inhibit the effects of known mutagens.[17,18]

Studies using extracts of Indian rhubarb have shown some similar anticarcinogenic effects. Particular interest has been focused on aloe emodin, an anthraquinone present in plants of the rhubarb family. This substance has been shown to have both tumour inhibition and tumour initiation properties.[19–22]

Slippery elm contains high concentrations of fatty acids and fatty acid esters. It has been used as a folk remedy for a wide variety of health complaints and as a preservative for certain fat-containing products. It is readily available in health food stores in products such as cough lozenges. Fatty acids and fatty acid esters similar to those in slippery elm have been shown to have cytostatic activity in cell systems and in mouse studies using Ehrlich ascites tumour cells.[11] These substances have also been shown to have an immunomodulatory effect in some animal studies.[14]

Very little information was found on sheep sorrel. It does not seem to have a history of use as a folk remedy, although a similar plant, yellow dock (*Rumex crispus*), has been used as a folk remedy for infections, bruises and burns.

## Conclusion

The review of all the information about Essiac for the task force reveals some weak evidence of its effectiveness and suggests that Essiac is unlikely to cause serious side effects when used as directed. However, the nature and quality of studies reporting benefit are such that the findings can only be regarded as preliminary. High-quality and open-minded research into the effects of this popular unconventional therapy is needed. The principal danger of this and other unconventional therapies is that they may delay the diagnosis and conventional treatment of serious disease. Also, although the cost of Essiac is not very great, it may cause hardship for some individuals. It is essential to maintain effective and open communication between patients and their physicians about unconventional therapies. The CBCRI and the Canadian Cancer Society are working to help address the need for research and for open communication in this area.

This article reports some of the work carried out by the Task Force on Alternative Therapies of the Canadian Breast Cancer Research Initiative (CBCRI). The CBCRI is the main funder of breast cancer research in Canada and was established in 1993 as a consortium of the Canadian Cancer Society (CCS), the National Cancer Institute of Canada (NCIC) — which also serves as the administrative home of the CBCRI — and the federal government (through the participation of the Medical Research Council of Canada and the National Health Research and Development Programme). In addition to the author, a number of other CBCRI staff worked on the project, including Dr. Carmen Tamayo (research associate), Ms. Rebecca McDonald and Ms. Jess Merber. Others contributed to the reviews of specific agents. The task force was chaired by Ms. Donna Cappon. Dr. Kaegi was the Director of Medical Affairs and Cancer Control for the CCS and the NCIC and staff partner with the task force.

Green tea will be the topic of the next article in the series, to appear in the Apr. 21 issue.

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Peer-reviewed journals dealing with unconventional therapies:
*Alternative Therapies in Health and Medicine*
*The Journal of Alternative and Complementary Medicine*



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