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Flor-Essence® Herbal Tonic Use in North America: A Profile of General Consumers and Cancer Patients

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ABSTRACT

Objectives: Flor-Essence® and Essiac™™ are widely used herbal tonics. After three decades, little is known about consumers using them. This pattern-of-use survey was conducted to 1) profile consumers, 2) characterize cancer patients, and 3) determine reasons for use, benefits, and adverse events.

Methods: A population-based study assessed Flor-Essence consumers in North America between June 1998 and August 1999. Data are presented in frequencies and proportions.

Results: Of 5,051 consumers (response 6.4%), most were Caucasian, educated, American, long-term users (mean 15.8 months, SD=17.4), and cancer patients. Of 1,577 cancer patients (response 42.4%), 85.3% were treated previously and 36.8% currently with conventional medicine for breast, prostate, or lung cancer. Overall, 64.5% discussed using the tonic with physicians; few (11.4%) exceeded the recommended dose. Most patients (50.6%) reported improvement in symptoms, but 6.6% experienced adverse events.

Conclusions: The tonic is widely distributed. Many cancer patients combine conventional treatment with the tonic and attribute benefits to the tonic. The use of herbal formulas is a public health issue; thus, assessment of clinical benefit and potential interaction with *cancer* treatment is warranted.

BACKGROUND

Flor-Essence and Essiac are two of the most widely used herbal tonics by cancer patients. An estimated 35% of cancer patients in Canada [1] use these tonics, whose long and controversial history spans three decades.[2,3] In a recent survey at a large comprehensive cancer center in the United States, 38% of patients reported using herbs and overall, 4.9% used the Flor-Essence or Essiac tonic.[4] Both formulas contain four principal herbs: burdock root (*Arctium lappa* L.), Turkish rhubarb root (*Rheum palmatum* L.), sheep sorrel *(Rumex acetosella* L.), and slippery elm bark (*Ulmus rubra* Muhl.). However, Flor-Essence contains four additional herbs that are believed to potentiate the formula: watercress (*Nasturtium officinale* R. Br.), blessed thistle (*Cnicus benedictus* L.), red clover (*Trifolium pratense* L.) and kelp (*Laminaria digitata* Lmx.). Flor-Essence tonic is manufactured in Canada where approximately forty thousand units of tonic and dried herbs are distributed to Canada and the United States each month.

A review of the literature on these tonics and the four principal herbs resulted in 107 references. Of those, 68% (n=73) were related to cancer.[5] Although 24 pre-clinical evaluations of individual herbs were reported, no pre-clinical or clinical trials of the tonic were identified.[5] One clinical study with Essiac was discontinued by the Health Protection Branch of Health Canada in 1978 because of limited physician participation. Data from 87 participants was considered inadequate to determine any impact on survival.[2] However, no toxicity was reported, but quality of life or pain control were not evaluated.[3,6] Subsequently, claims for clinical benefit were discontinued by the manufacturers who then began marketing the product as a dietary supplement with general health claims (i.e., prevent disease, relieve pain, and improve quality of life).

Claims as a cancer cure persist, however, with anecdotal reports of reduced tumor growth, improved quality of life, and prolonged survival.[7] Although these tonics remain untested for anticancer activity, antioxidant activity has been confirmed for the Flor-Essence product.[8]

Moreover, qualitative thin layer chromatography (TLC) has confirmed seven herbs that contain trace elements, minerals, and phytoestrogens.[9] Levels of flavonoids, phenylcarboxylic acids, and emodin are monitored regularly in each batch.

Pre-clinical and clinical evaluations of Flor-Essence, in collaboration with the Russian Ministry of Health, have assessed acute and chronic toxicity. Acute toxicity studies were unable to determine a lethal dose in albino mice and rats. Furthermore, chronic toxicity tests found no renal or hepatic toxicity doses that were 10-fold the therapeutic dose (15 ml/kg) in albino mice and rats and 5-fold (7.5 ml/kg) in dogs.[10] Sponsor initiated in vivo studies report reduced number and size of chemical mediated gastric ulcerations, protection of capillaries against xylene-mediated leakage, and prevention of chemically induced anti-inflammation.[9]

Given the historical and widespread use of these tonic, limited preclinical data by manufacturers only, and the anecdotal reports of efficacy from cancer patients, a pattern of use survey of Flor-Essence consumers and cancer patients was conducted to 1) profile the general consumers, 2) characterize cancer patients, and 3) determine their reasons for use, perceived benefits, and adverse events. Ultimately, this information will inform the medical community and cancer patients, stimulate manufacturers to prepare the tonics for clinical investigation with an Investigational Drug Application (IND), and guide the development of clinical trials with information about which cancer patients are more likely to use the product.

METHODS

Individuals who purchased Flor-Essence in the United States or Canada between June 1998 and August 1999 were invited to participate, regardless of age, gender, or disease status. The Committee for the Protection of Human Subjects at the University of Texas-Houston approved the study at two levels; participation was voluntary.

The manufacturers shipped 20,000 units of product in Canada and 65,245 in the United States over a three month period, beginning in June, 1998. Each product contained an invitation from the owner of Flora Manufacturing and Distributing Ltd. (Burnaby, B.C.) to participate so that the company could learn more about who is using the product and why. Each product contained a self-addressed, stamped postcard with the brief pattern of use survey. To ensure confidentiality, each postcard contained a unique identification number.

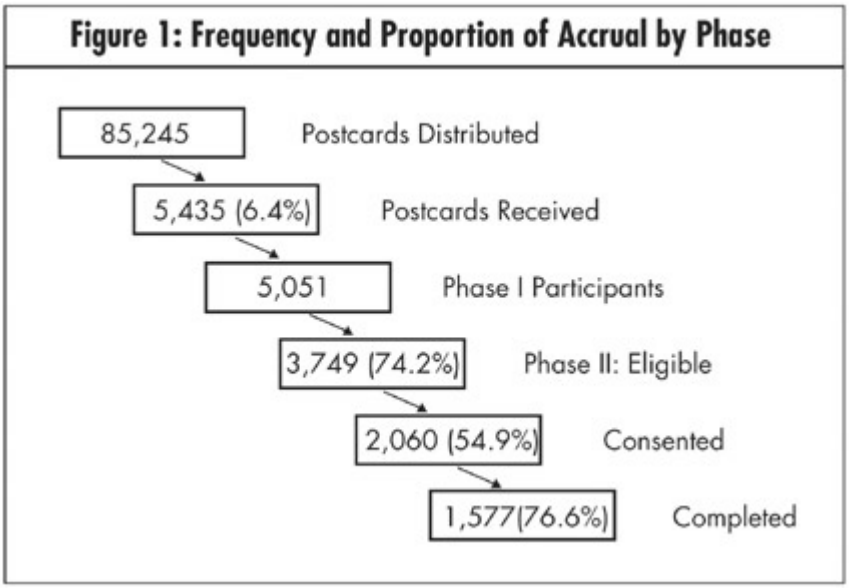
For Phase I, the pattern of use survey of general consumers collected information on demographics (i.e., age, gender, ethnicity, country of residence, marital status, education level, and household income), medical condition (i.e., arthritis, cancer, multiple sclerosis, or other), reasons for use (i.e., prevention, control symptoms, treat a medical condition, or other), duration of use, and perceived benefits using a 5-point rating scale from excellent to poor.

Current or former cancer patients were invited to call the University of Texas Center for Complementary and Alternative Medicine (UT-CAM) about the details of a second survey, specifically about their experience with the tonic. For Phase II, interested individuals who telephoned UT-CAM and were current or former cancer patients were invited to participate. After obtaining verbal consent, research assistants collected contact information to mail the coded survey. Callers who declined to participate or who were ineligible were encouraged to complete and return the postcard. Flora Manufacturing and Distributing Ltd. provided one complimentary product to individuals who completed the cancer-specific survey.

The cancer-specific survey was adapted from an instrument that assessed complementary and alternative medicine (CAM) use in a comprehensive cancer center.[11] Cancer patients who were using the tonic provided information on their cancer status (i.e., date of diagnosis, stage and site of disease, current status), conventional treatment (i.e., chemotherapy, radiation, surgery, hormonal), and use of other CAM therapies. We also asked about their reasons and expectations for using Flor-Essence as well as information on dose, frequency, adverse events, positive effects, changes in symptoms (i.e., nausea, vomiting, loss of appetite, fatigue, pain). For patients who discussed use with their physicians, we asked how the physicians responded; otherwise, patients explained their reasons for nondisclosure about the herbal use.

Eligibility and consent rate

Of the 85,245 units distributed, 5,435 (response rate = 6.4%) postcards were received for Phase I. A total of 384 general consumers were excluded because they were treating pets (n = 38) or responded after the study closed (n = 346) in September, 1999. Of the 5,051 eligible general consumers, 3,749 (74.2%) were eligible for Phase II. Of these, 54.9% (n = 2,060) cancer patients consented to participate, and 1,588 (42.4%) completed the survey; however, 11 individuals were excluded because they responded after the study closed.



Phase I: Profile of General Consumers

The majority of Flor-Essence consumers were educated above the high school level (63.6%), Caucasian (92.0%), married (68.8%), living in the United States (80.0%), 61.6 years of age (SD = 13.9), and approximately equally distributed by gender (Table 1.). The average duration of use was 15.79 months (SD = 17.35, range 0-130 months), and primarily (62.4%) to treat a medical

condition rather than prevent disease (35.3%) or control symptoms (21.3%). Cancer was the most commonly reported medical condition (75.1%), but general consumers' other health conditions were arthritis (14.5%), multiple sclerosis (1.0%), and other (14.7%) conditions (i.e., allergies/asthma, chronic fatigue, cysts, diabetes, high blood pressure/heart disease, hepatitis/liver disease, osteoporosis, or bladder, prostate, skin, or stomach problems). Most consumers rated the benefits of the tonic as very good/excellent (72.2%), but 24.4% rated the tonic as okay, and 3.4% as not very good/poor.

Table 1. Demographic Profile of Consumers & Cancer Patients

	Consumers (n = 5,051)		Cancer Patients (n = 1,211)*	
Variable	**n**	**%**	**n**	**%**
Gender				
Women	2693	54.3	625	52.2
Men	2262	45.7	572	47.8
(Missing)	*(96)*	—	*(14)*	—
Ethnicity				
Caucasian	4511	92.0	1118	94.1
African-American	119	2.4	22	1.9
Asian	111	2.3	27	2.3
Hispanic	104	2.1	12	1.0
Other	59	1.2	9	.8
(Missing)	*(147)*	—	*(23)*	—
Marital status				
Married	3455	68.8	867	71.9
Widowed	554	11.0	120	10.0
Divorced	438	8.7	99	8.2
Single/never married	310	6.2	67	5.6
Living with partner	190	3.8	37	3.1
Separated	72	1.4	14	1.2
Other	2	0.0	2	0.2
(Missing)	*(30)*	—	*(5)*	—
Education				
High school or less	1790	36.4	427	36.1
Some college	1371	27.9	309	26.1
College graduate	995	20.3	268	22.6
Postgraduate study	756	15.4	180	15.2
(Missing)	*(139)*	—	*(27)*	—
Country of Residence				
United States	3895	80.0	941	79.9
Canada	976	20.0	237	20.1
(Missing)	*(180)*	—	*(33)*	—

*Surveys and postcards could not be matched to obtain demographic data for 366 cancer patients.
n = number

Phase II: Profile of Current and Former Cancer Patients

Demographics of Cancer Patients

Surveys and postcards were matched for 76.8% (n=1,211) of respondents in Phase I and II; thus, data on demographics were unavailable for 366 cancer patients. Flor-Essence was used equally by men and women, but most individuals were educated above the high school level (63.9%), Caucasian (94.1%), married (71.9%), living in the United States (79.9%), and 62.4 years of age (SD = 13.1) (Table 1).

Disease Status and Treatment Profile of Cancer Patients

Overall, 63.9% of cancer patients had been diagnosed over a 3-year period (i.e., 30.0% in 1998, 20.9% in 1997, 13.0% in 1996) for breast (22.0%), prostate (15.1%), or lung (10.6%) cancer. At

the time of diagnosis, patients were equally distributed across stage I to IV disease; 33.7% reported metastatic disease. Of the 274 (19.0%) who reported "other" stage of disease at diagnosis, 49.8% did not know the stage. At the time of the survey, however, 38.9% of the respondents reported having no evidence of disease. Of the 365 (26.5%) who reported "other" stage of disease at the time of the survey, 58.6% did not know the stage (Table 2).

Table 2. Stages of Disease at Diagnosis and Time of Survey

	Time of Staging	
Stage of Disease	**Diagnosis (%)**	**Survey (%)**
I	24.3	8.9
II	18.8	6.1
III	19.0	6.4
IV	18.8	13.2
Other	19.0	26.5
No evidence of disease	N/A	38.9

At the time of their last check-up, 40.6% of participants stated they were told they had no evidence of disease. The remainder of participants stated their disease was regressing (14.6%), stable (13.9%), or progressing (15.5%); however, 9.9% did not know their disease status.

Most (88.7%) patients had received previous conventional cancer treatment, including surgery (51.4%), chemotherapy (46.6%), radiation therapy (36.7%), hormonal (15.1%), or other (11.3%) approaches. Of the 175 individuals who reported "other" approaches, 70.3% were CAM treatments. Therefore, 85.3% actually had received conventional treatment. At the time of the survey, most patients (60.9%) were currently being treated with the following: surgery (2.5%), chemotherapy (18.6%), radiation (3.4%), hormonal approaches (14.2%), or other therapies (29.9%). Of the 460 (29.9%) who reported receiving "other" therapies, 3.7% cited immune therapies while 90.2% were using CAM treatments. Therefore, only 36.8% actually were receiving conventional treatment at the time of the survey.

Duration of Use and Dose Information

At the time of the survey, almost all (98.3%) respondents were using Flor-Essence, and most (61.2%) had used the tonic for at least 6 months. Specifically, 44.7% had used the tonic for more than 12 months, 16.5% for 6 to 12 months, 32.7% for 1 month to less than 6 months, and 6.1% for less than one month.

Most patients (85.0%) reported that the instructions were adequate, but 15.0% stated that information was inadequate in general (n = 49) and specifically, inadequate regarding dose instructions (n = 39), duration of treatment (n = 31), and supporting research (n = 22). Overall, 30.4% (n = 475/1,551) reported following the recommended dose (i.e., 4 ounces or less daily). For the 1,079 patients who provided information on dose, 19.6% (n = 212) stated that they followed the instructions, but 12 individuals exceeded the recommended daily dose by using 4.5 to 10 ounces daily. Of the 867 patients (80.3%) who reported not following instructions, the majority (n = 756) actually followed the recommended guidelines, but 111 individuals exceeded the recommended dose by using 4.5 to 32 ounces daily. Thus, 11.4% (n = 123/1,079) of current or former cancer patients exceeded the recommended dose, but most (88.6%) followed the dose instructions (Table 3).

Table 3.
Compliance with Dose Instructions for Flor-Essence (n = 1,079)

Used Correct Dose (< 4 ounces/day)	Reported Following Dose Instructions: Yes	No	Total
Yes	200	756	956
No	12	111	123
Total	212	867	1,079

Reasons for Use, Expectations, and Perceived Benefits and Adverse Events

Most cancer patients (84.9%) used the tonic because they believed it could help, and 23.7% because they were told that their cancer was incurable. Other reasons included the following: the tonic is nontoxic (56.4%), provides hope (50.4%), allows control over medical care decisions (39.8%), and other reasons (18.7%). Of the 294 who reported other reasons, the most common reasons were the recommendation by family or friends (34.6%) or belief in possible disease control (17.5%).

Most patients (76.5%) expected the tonic to improve their immune system, and others expected the tonic to improve survival (59.4%) or quality of life (53.2%), cure their cancer (48.9%), or relieve symptoms (28.6%). Of the 8.5% (n = 133) who cited other reasons, 63 expected Flor-Essence to control or prevent disease. The perceived benefits of the tonic reported by cancer patients were comparable to those of consumers since 75.5% of consumers were cancer patients. Cancer patients rated the benefits from very good/excellent (71.0%) and okay (27.1%) to not very good/poor (2.8%). Most patients (86.7%) reported positive effects, including the following: felt better (53.2%), no cancer progression (40.6%), able to carry out daily activities (34.0%), more energy (31.5%), coped better with the disease (26.3%), improved cancer symptoms (22.3%), and cured their cancer (16.2%).

Overall, 50.3% (n = 584/1162) reported an improvement in a symptom while using the tonic, including improvements in fatigue (29.8%), appetite loss (15.0%), nausea (8.4%), pain (11.6%), vomiting (4.1%), and other symptoms (12.4%). However, 6.6% (n = 103/1560) reported ill effects with Flor-Essence. Overall, the most frequently reported adverse events were diarrhea (1.9%), constipation (1.2%), nausea (1.1%), and fatigue (0.9%).

Other Therapies and Disclosure to Providers

Most participants used CAM approaches simultaneously with the tonic including high dose vitamins and antioxidants (61.5%), other herbs and herbal mixtures (41.6%), special diets (41.4%), spiritual practices (35.0%), movement and physical therapies (21.5%), mind/body therapies (20.4%), and other CAM therapies (19.5%).

Most patients learned about this tonic from family and friends (65.1%), but other sources of information included books and magazines (35.1%), other cancer patients (18.4%), CAM practitioners (15.0%), doctors (4.3%), nurses (2.0%), social workers (0.2%), and other sources (14.6%). Of these 229 patients who learned of Flor-Essence from other sources, 55.9% were advised by health store personnel or nutritionists and 14.1% from the Internet.

Most patients (64.5%) discussed CAM use with their health care provider, and of those, 49.6% talked with their oncologists. Patients also discussed CAM use with their primary care physician (28.6%), nurse (13.1%), and social worker or psychiatrist (3.7%). During these discussions, patients perceived the providers to be either neutral (54.4%) or encouraging (40.5%). Few stated they were warned of risks (8.4%) or advised to discontinue the tonic (4.0%). Of the other responses cited (18.4%), participants reported that providers responded with "I don't believe in CAM" (n = 44) or "It probably won't hurt" (n = 36).

For the 559 patients who did not discuss CAM use with providers, the most common reasons were related to physicians: doctors never asked (62.3%), would discourage/disapprove (28.9%), or would not understand (26.7%). Others felt it was not important for physicians to be informed (25.0%) or were unsure if CAM was beneficial (11.9%). Only 5.9% believed that disclosure of CAM use resulted in the physician discontinuing the relationship.

DISCUSSION

This cross-sectional study is the first in North America to systematically assess the general pattern of use for Flor-Essence herbal tonic and specifically, to document the experience of cancer patients. This study found that consumers were predominately cancer patients, had used the tonic long term to treat a medical condition, and perceived the tonic as highly beneficial. Overall, they were predominately Caucasian, educated beyond high school and thus, characteristic of cancer patients who use CAM.[12-14] These patients in this survey were older and thus, not typical of cancer patients in general who use CAM,[15-25] although several studies report no association with age and CAM use.[13,26-28] Most participants had been diagnosed with breast, prostate, or lung cancer, but approximately one-quarter were unaware of their disease stage at the time of diagnosis or the survey.

Although this convenience sample represents a self-selected group of cancer patients, over 60% had used the herbal mixture for greater than 6 months. The reasons for using the tonic were consistent with other surveys of cancer patients. Most patients use CAM approaches to gain hope and improve quality of life;[29] however, one-quarter turned to this CAM approach after learning their cancer was not curable.[23,30] We also found that many cancer patients combined the tonic with conventional treatment. The finding is consistent with the literature that indicates that few patients abandon conventional cancer care for CAM[14] whereas 60-80% combine CAM and conventional treatment.[12,13,18,19,24,27,29,31-35] The literature also suggests that physicians are interested[36,37] and willing to discuss CAM therapies with their patients, but want scientific evidence of efficacy and safety.[38] We found that most cancer patients discussed using the tonic with their physician; however, the majority who did not talk with physicians cited attitude of the physician as the primary reason for their nondisclosure.

Although several herbs have demonstrated anticancer, cytotoxic, and immunomodulatory activity,[9] clinical evidence to support the use of this agent is lacking as is data on possible interactions of Flor-Essence with conventional treatment. The majority of cancer patients reported following instructions; however, 11.4% were exceeding the recommended daily dose. In fact, 6.6% reported adverse events, including nausea, vomiting, and diarrhea. Of those who reported side effects, however, 11.8% reported that they exceeded the recommended daily dose. Despite the absence of scientific evidence, cancer patients expected the tonic to increase or improve the activity of their immune system, and many expected the tonic to improve survival and quality of life. The major sources of information were family, friends, and anecdotal reports.

Assessment of efficacy and safety by carefully controlled prospective clinical trials is critical. As a result of this pattern of use survey, a pilot study is planned to determine the feasibility of accruing patients who are presenting for palliative chemotherapy for Stage IV colon cancer to receive the herbal tonic or placebo. The pilot will provide experience in the context of integrated care to assess CAM. If successful, the preliminary data on quality of life, general health outcomes (i.e.,

pain, weight, and performance status), safety, and tolerability will provide the basis for a larger, more definitive trial. Such a study, however, would need sufficient power and long-term follow-up to determine efficacy using a full range of outcomes, including disease progression.

Limitations

As with all self-selected populations, this sample may be representative of more enthusiastic and committed consumers and thus, may be biased and not representative of the Flor-Essence consumer in general. However, these interesting results suggest the need for more representative samples. The response rate among eligible cancer patients was 42.4% and lower than rates for mailed surveys of CAM use among cancer patients in Italy (51.2%) and the United Kingdom (69%).[15,23] No study that we are aware of has attempted to conduct a pattern of use survey of CAM users by targeting consumers of an herbal product. Thus, we are unable to compare our response rate with those from similar studies.

Conclusion

This study confirmed that the widespread use of CAM is a reality and may reflect unmet patient needs within the current model of health care. These patients were clearly seeking hope and an opportunity to enhance their clinical outcome by expanding their treatment options. This behavior was reflected among general consumers as well. Since 1990, the prevalence of CAM use in the United States has increased to 42%, visits to CAM practitioners have risen to 629 million, and out-of-pocket expenditures climbed to $34.4 billion.[39] In 1997, sales in the U.S. jumped 70% to $3.24 billion for herbs, and some $27 billion was spent in the U.S. on CAM therapies in general, with two-thirds of that money paid out-of-pocket.[39]

Regulatory requirements for the approval of prescription drugs require a review and analysis of clinical data for drug development, but botanicals differ from chemically produced drugs. These products are sold as dietary supplements rather than therapeutic agents. These herbal tonics consist of multiple herbs, each containing multiple constituents with known compounds, both active and inactive, as well as unknown compounds and elements, which may be active or inactive. The mechanism of action is usually unknown and variability within the same plant material usually high, thus challenging the ability for standardization and stability.[40] Regardless, the Flor-Essence tonic has a long history of sustained use over the past decades. Consumers believe they benefit from this product. Given the widespread use by cancer patients, regardless of clinical benefit, rigorous assessment by the conventional medical community is the next logical step to better inform patients and their physicians.

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