

## USE OF HERBAL REMEDIES AMONG CANCER AND TRANSPLANT PATIENTS IN THE TOWN OF PALERMO, SICILY

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*[Uso di erbe medicinali in pazienti neoplastici e trapiantati. Uno studio condotto nella città di Palermo]*

### SUMMARY

Concomitant use of herbal remedies may lead to toxicity or failure of conventional therapies in different patients. The objectives of this survey were to assess: (1) the prevalence of the use of vegetal remedies by cancer and transplanted patients (2) the level of communication about such use to the physicians (3) whether such use might be associated to adverse reactions or interactions with conventional drugs.

The study was carried out on 100 consecutive cancer patients attending the outpatient medical oncology clinic of the University Hospital "P. Giaccone", Palermo and on other 100 transplanted patients who were hospitalized or followed up at ISMETT, Palermo. Another group was composed of 248 relatives of patients interviewed at ISMETT.

Among cancer patients, 6 referred a current use of vegetal remedies (in particular *Aloe* in 4 cases and fennel in two), while 28 referred a previous use. Among transplanted patients, 4 and 13 referred current and previous use of vegetal remedies, respectively. Of the other subjects interviewed, 8 and 68 referred current and previous use of vegetal remedies, respectively. There was not so a substantial change in the use of herbal products with the onset of the disease, which could demonstrate a major concern for the efficacy of conventional treatments. No patient or subject reported a current or previous usage of *Hypericum*. 83.3% of cancer patients, 50% of transplanted patients and 87.5% of the other subjects referred having communicated the current use of vegetal remedies to their physicians. Overall, we have verified that in a Sicilian sample of cancer and transplanted patients the use of herbal remedies is relatively low and with characteristics not alarming in terms of significant toxicities or interactions with conventional drugs.

**Key words:** Herbal medicines, oncology, trasplantation, adverse reactions, interactions, aloe

### RIASSUNTO

*L'uso concomitante di erbe medicinali può portare a tossicità o insuccesso delle terapie convenzionali in differenti pazienti. Obiettivi di questa indagine sono stati quelli di appurare: (1) la prevalenza dell'uso di rimedi vegetali tra i pazienti neoplastici e trapiantati; (2) se i pazienti informano i loro medici riguardo a tale uso; (3) se tale uso è associato a reazioni avverse o interazioni con farmaci convenzionali.*

*Lo studio è stato condotto su 100 consecutivi pazienti neoplastici afferenti al Day Hospital di Oncologia Clinica del Policlinico Universitario "P. Giaccone" di Palermo e su altri 100 pazienti trapiantati ricoverati o seguiti all'ISMETT di Palermo. Un altro gruppo è stato composto da 248 familiari di pazienti intervistati all'ISMETT.*

*Tra i pazienti neoplastici, 6 hanno riferito l'uso corrente di rimedi vegetali (in particolare Aloe in 4 casi e finocchio in 2), mentre 28 hanno riferito un uso precedente. Tra i pazienti trapiantati, 4 e 13 hanno riferito un uso corrente e precedente di rimedi vegetali, rispettivamente. Degli altri soggetti, 8 e 68 hanno riferito un uso corrente e precedente di rimedi vegetali, rispettivamente. L'insorgenza della malattia non ha determinato modificazioni nell'uso di prodotti di erboristeria tali da indicare una mancanza di fiducia nei trattamenti convenzionali. Non è stato registrato alcun uso di Hypericum.*

*83,3% dei pazienti neoplastici, 50% dei trapiantati e 87,5% degli altri soggetti hanno riferito di avere informato i medici riguardo al loro uso corrente di erbe medicinali. Nel complesso, abbiamo accertato che in un campione siciliano di pazienti neoplastici e trapiantati l'uso di erbe medicinali è relativamente basso e non allarmante in termini di significative tossicità o interazioni con farmaci convenzionali.*

**Parole chiave:** Erbe medicinali, oncologia, trapianti, reazioni avverse, interazioni, aloe

### Introduction

The use of complementary and alternative medicine (CAM), defined as a group of different medical and health care systems, practices and products not considered part of conventional medicine,

is widely diffused. CAM includes numerous approaches, like for example traditional Chinese, Ayurvedic and other folk medicines, and very often turns to herbal remedies<sup>(1-3)</sup>.

Generally, common people believe that natural products are safer than conventional drugs.

However, these remedies are rarely tested and monitored for clinical safety and effectiveness and scarcely governed by regulations setting their composition and purity, so that their effects are often unpredictable<sup>(4-6)</sup>. The issue of the interactions between herbal products and conventional drugs is of great interest, since the former substances may, through several mechanisms, lead to failure or enhanced toxicity of the established therapies. However, often CAM usage is the result of self-diagnosis and self-prescription and, even if the patients may be informed about the need to communicate this practice to the physicians, they rarely do it<sup>(7-9)</sup>.

Patients with an increased likelihood of undesired problems from the use of herbal products include cancer and transplanted patients owing to their underlying conditions and to the long-term exposure to low therapeutic index agents such anti-cancer or immunosuppressive drugs. However, the prevalence of herbal medicine use among cancer patients has been estimated to between 7% and 13%<sup>(10)</sup>. The motivations include the beliefs to alleviate symptoms of cancer, counteract the adverse effects of chemotherapy or improve the immune system response<sup>(10-13)</sup>. Also transplant patients can regularly use herbal products<sup>(14-16)</sup>.

For example, in a recent study Hess S. et al.<sup>(17)</sup> reported that in Switzerland 11.8% (42/356) of renal transplant patients use one or more forms of CAM remedies: in particular 2.5% (9/356) use Bach flower remedies, 1.9% (7/356) herbal remedies and 0.3% (1/356) Tibetan herbs. In addition, 0.6% (2/356) use St. John's wort (*Hypericum perforatum*), reputed as a mild antidepressant, but that can interfere with the immunosuppressive calcineurine inhibitors and other therapies through the induction of cytochrome P-450 enzymes<sup>(17)</sup>. In another study performed in USA, 15.6% (5/32) liver transplant patients used herbal products, which included milk thistle (silymarin), *Eclipta* and green beet leaf, all considered as "hepatic tonics"<sup>(18)</sup>.

The present paper is a preliminary survey of the use of vegetal remedies in cancer or transplanted patients undergoing chemotherapeutic or immunosuppressive treatments in two hospitals of the town of Palermo, Sicily, Italy. The principal objectives were to assess: 1) the prevalence of the use of vegetal remedies among the patients; (2) the level of communication about the use of such practice to the physicians; (3) whether the use of vegetal remedies might be associated to adverse reactions or interactions with conventional drugs<sup>(19-21)</sup>.

## Patients and methods

### Study population

The study was carried out on 100 consecutive cancer patients attending the outpatient clinic at the Medical Oncology Unit of the Policlinic "Paolo Giaccone", University of Palermo and on other 100 transplant patients who were hospitalized or followed up at the "Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione (ISMETT)", Palermo. Another group was composed of relatives of patients interviewed at ISMETT. People who participated to the study were informed about the scopes of the study and consented to its realization through a questionnaire administered by an interviewer.

### Questionnaire

The questionnaire recorded general information on patients like age, sex, place of residence, educational background, smoking and alcohol habits. Questions about CAM were about the current or previous use of homeopathy, acupuncture, Chinese, Ayurvedic and other folk medicines, Back flowers and other herbal remedies, integrators and vitamins. Patients were also asked whether their physicians were informed of the use of such products as well as about possible adverse reactions encountered from their use.

## Results

The general data of patients are reported in Table 1.

6% of cancer patients referred a current use of herbal remedies, while 28% referred a previous use. Among transplant patients, 4% and 13% referred current and previous use of herbal remedies, respectively. Of the other subjects interviewed 3.2% and 27.4% referred current and previous use of herbal remedies, respectively.

In general, current and previous use of herbal remedies was more pronounced in females than in males (Table 2).

The herbal remedies more currently used were *Aloe*, by 4 cancer patients, and combinations including fennel, by 2 cancer patients (Table 3). The herbal remedies used previously are presented in Table 4.

83.3% (5/6) of cancer patients, 50% (2/4) of transplant patients and 87.5% (7/8) of the other subjects had informed their physicians about the current use of herbal remedies (Table 5).

		CANCER PATIENTS	TRASPLANT PATIENTS	OTHER SUBJECTS
NUMBER OF PATIENTS	Total	100	100	248
	Men	40	70	116
	Women	60	30	132
AGE	Median	60	51	44.9
	Range	31-80	14-76	13-81
EDUCATION	Primary school degree	42%	18%	11%
	Secondary school degree	22%	31%	25%
	High school degree	25%	47%	44%
	Graduated	11%	4%	20%
PLACE OF RESIDENCE	Country	14%	34%	34%
	Town	10%	14%	18%
	City	76%	52%	48%
TOBACCO USE		14%	15%	24%
ALCOHOL USE		24%	10%	12.5%

**Table 1:** General data of the subjects

In cancer patients and, at a lesser extent, in transplant patients the use of herbal remedies was correlated with a higher instruction level (Tables 6 and 7).

Tobacco smoking habits were not particularly different in the current users of herbal remedies compared to the non-users. Instead, alcohol use was higher in the patients who used herbal remedies.

In fact, 66.6% of cancer patients who currently used herbal remedies and 21.3% of those who did not reported to consume alcoholic drinks. For transplant patients, the respective percentages were 25% and 9.3% respectively, and for the other subjects they were 25% and 10.4% (Tables 8 and 9).

**Discussion and conclusions**

Natural and alternative remedies are often considered as safe and effective, but people is unaware of possible adverse effects associated to their use.

Differently from other studies, which have reported that the use of herbal remedies is common in cancer and transplant patients<sup>(22-26)</sup>, our results are not so alarming; in fact, such use was relatively low among the subjects who participated in the study, possibly demonstrating a substantial faith in conventional treatments. The low rate of use in transplant patients might be due also to other reasons, including the fear of damaging the new organ as well as the large number of medications and supplements that the patient is already required to take.

As reported also by other studies<sup>(27, 28)</sup>, the use of herbal remedies resulted to be progressively correlated to a higher level of instruction. Encouragingly, a good part of our patients had informed their physicians about such use. This communication is indeed necessary to prevent possible harmful effects and interactions with conventional drugs; it is probably also for this reason that herbal remedies did not seem to have caused any problem in the patients.

*Aloe*, the herbal medicine more commonly used by our patients, is often employed as a laxative or as an anticancer agent, even though these indications are not supported by definitive scientific evidences<sup>(29)</sup>.

Long term use of *Aloe* may induce hypokalemia, which potentiates, with possible induction of toxicity, the activity of cardiac glycosides or of antiarrhythmic drugs, like quinidine, which prolongs the Q-T interval in ECG<sup>(30)</sup>.

	Cancer patients			Transplant patients			Other subjects		
	All	Males	Females	All	Males	Females	All	Males	Females
Current herbal remedies use	6/100 (6.0%)	2/40 (5.0%)	4/60 (6.6%)	4/100 (4.0%)	3/70 (4.2%)	1/30 (3.3%)	8/248 (3.2%)	0/116 (0%)	8/132 (6.0%)
Previous herbal remedies use	28/100 (28.0%)	5/40 (12.5%)	23/60 (38.3%)	13/100 (13.0%)	8/70 (11.4%)	5/30 (16.6%)	68/248 (27.4%)	15/116 (12.9%)	53/132 (40.1%)

**Table 2:** Herbal remedies use

Cancer patients	Transplant patients	Other subjects
<ul style="list-style-type: none"> <li>• Aloe (n=4)</li> <li>• Mint, fennel, liquorice, tea (n=1)</li> <li>• Phyllanthus niruri, camomile, mallow, fennel (n=1)</li> </ul>	<ul style="list-style-type: none"> <li>• Camomile (n=1)</li> <li>• “Ten Herbs” (n=1)</li> <li>• Unspecified (n=2)</li> </ul>	<ul style="list-style-type: none"> <li>• Aloe vera, mallow, green tea + Bach flowers (n=1)</li> <li>• Aloe, Cassia, Taraxacum (n=1)</li> <li>• Cassia, Fucus (n=1)</li> <li>• Cascara (n=1)</li> <li>• Red grapevine (n=1)</li> <li>• Unspecified (n=3)</li> </ul>

**Table 3:** Current herbal remedies use

Cancer patients	Transplant patients	Others subjects
<ul style="list-style-type: none"> <li>Fennel (n=2)</li> <li>Aloe ferox, Genziana, fennel, liquorice, Senna, dandelion, rhamnus, rhubarb, weed, Cascara sagrada (n=1)</li> <li>Fennel, peppermint, liquorice (n=1)</li> <li>Fennel, Carum carvi, anise, cumin, peppermint, liquorice, valerian (n=1)</li> <li>Fennel, soy, green tea, camomile, malva, propolis (n=1)</li> <li>Fennel, Phyllanthus niruri, camomile, mallow (n=1)</li> <li>Phyllanthus niruri (n=2)</li> <li>Camomile (n=1)</li> <li>Hawthorn (n=1)</li> <li>Green tea (n=1)</li> <li>Green tea, red grapevine, dandelion (n=1)</li> <li>Horse chestnut, green tea, Melilotus, vitamin C (n=1)</li> <li>Aloe (n=1)</li> <li>Aloe arborescens, mallow, Fucus, liquorice, dandelion (n=1)</li> <li>Mallow (n=1)</li> <li>Fibres, unsaturated fatty acid (omega 9-6-3), lignans (Linaza), prickly pears, weed (n=1)</li> <li>Guaranà, Ginkgo biloba, Eleutherococcus (n=1)</li> <li>Carnation, cinnamon, nutmeg (n=1)</li> <li>Artichoke (n=1)</li> <li>Rosemary (n=1)</li> <li>Algal oil, vitamin C, vitamin E, zinc, cuprum, lutein, zeaxanthin, tocotrienols (n=1)</li> <li>Bach flowers (n=1)</li> <li>Unspecified (n=4)</li> </ul>	<ul style="list-style-type: none"> <li>Fennel, Cascara, Aloe, liquorice, Senna (n=1)</li> <li>Green tea (n=1)</li> <li>Green tea, blueberry, rosehip (n=1)</li> <li>Hawthorn, mallow (n=1)</li> <li>Unspecified (n=9)</li> </ul>	<ul style="list-style-type: none"> <li>Fennel (n=1)</li> <li>Fennel, mallow (n=1)</li> <li>Fennel, birch (n=1)</li> <li>Camomile (n=2)</li> <li>Camomile, mallow, prickly pears, green tea (n=1)</li> <li>Camomile, hawthorn, mallow, (n=1)</li> <li>Camomile, mallow, laurel, prickly pears (n=1)</li> <li>Green tea (n=4)</li> <li>Green tea, Hieracium Pilosella (n=1)</li> <li>Aloe (n=1)</li> <li>Mallow (n=1)</li> <li>Prickly pears, Lespedeza capitata, Opuntia (n=1)</li> <li>Red grapevine (n=1)</li> <li>Arnica, blueberry, hawthorn (n=1)</li> <li>Valerian (n=2)</li> <li>Valerian, passion flower (n=1)</li> <li>Blackcurrant (n=1)</li> <li>Bach Flowers (n=4)</li> <li>Hieracium pilosella (n=1)</li> <li>Hieracium pilosella, birch (n=1)</li> <li>Cascara (n=1)</li> <li>Senna, Fucus (n=1)</li> <li>Soy (n=1)</li> <li>Tyme, rosemary (n=1)</li> <li>Blueberry (n=1)</li> <li>Taraxacum (n=1)</li> <li>Oats (n=1)</li> <li>Ananas (n=1)</li> <li>Unspecified (n=32)</li> </ul>

Table 4: Previous herbal remedies use

The concomitant use of *Aloe* with other drugs which induce hypokalemia (e.g. diuretics, adrenocorticosteroids and liquorice) may enhance electrolyte imbalance. However, no one of our patients did use these drugs concomitantly to *Aloe*.

Unlike other populations<sup>(31)</sup>, no one of our interviewed subjects referred the use of *Hypericum*, underlining the importance of the local habits and traditions as it regards the use of particular herbal remedies.

	Cancer patients			Transplant patients			Other subjects		
	All	Males	Females	All	Males	Females	All	Males	Females
Yes	5/6 (83.3%)	1/2 (50%)	4/4 (100%)	2/4 (50%)	1/3 (33.3%)	1/1 (100%)	7/8 (87.5%)	0/0 (0%)	7/8 (87.5%)
Not	1/6 (16.6%)	1/2 (50%)	0/4 (0%)	2/4 (50%)	2/3 (66.6%)	0/1 (0%)	1/8 (12.5%)	0/0 (0%)	1/8 (12.5%)

Table 5: Communication to physician about current use of herbal remedies

	Cancer patients			Transplant patients			Other subjects		
	All	Males	Females	All	Males	Females	All	Males	Females
Graduated	2/11 (18.1%)	1/5 (20.0%)	1/6 (16.6%)	0/4 (0%)	0/4 (0%)	0/0 (0%)	1/50 (2%)	0/24 (0%)	1/26 (3.8%)
High school degree	3/25 (12.0%)	1/9 (11.1%)	2/16 (12.5%)	2/47 (4.2%)	1/29 (3.4%)	1/18 (5.5%)	2/108 (1.8%)	0/54 (0%)	2/54 (3.7%)
Intermediate school degree	1/22 (4.5%)	0/6 (0%)	1/16 (6.2%)	2/31 (6.4%)	2/26 (7.7%)	0/5 (0%)	3/62 (4.8%)	0/26 (0%)	3/36 (8.3%)
Elementary school degree	0/42 (0%)	0/20 (0%)	0/22 (0%)	0/18 (0%)	0/11 (0%)	0/7 (0%)	2/28 (7.1%)	0/12 (0%)	2/16 (12.5%)

Table 6: Herbal remedies use and instruction (Current use)

	Cancer patients			Transplant patients			Other subjects		
	All	Males	Females	All	Males	Females	All	Males	Females
Graduated	6/11 (54.5%)	2/5 (40.0%)	4/6 (66.7%)	1/4 (25%)	1/4 (25%)	0/0 (0%)	16/50 (32%)	5/24 (20.8%)	11/26 (42.3%)
High school degree	10/25 (40.0%)	3/9 (33.3%)	7/16 (43.7%)	3/29 (10.3%)	3/29 (10.3%)	4/18 (22.2%)	26/108 (24.1%)	6/54 (11.1%)	20/54 (37%)
Intermediate school degree	6/22 (27.2%)	0/6 (0%)	6/16 (37.5%)	5/31 (16.1%)	4/26 (15.4%)	1/5 (20%)	19/62 (30.6%)	4/26 (15.4%)	15/36 (41.6%)
Elementary school degree	6/42 (14.2%)	0/20 (0%)	6/22 (27.2%)	0/18 (0%)	0/11 (0%)	0/7 (0%)	7/28 (25%)	0/12 (0%)	7/16 (43.7%)

Table 7: Herbal remedies use and instruction (Previous use)

	Cancer patients			Transplant patients			Other subjects		
	All	Males	Females	All	Males	Females	All	Males	Females
Tobacco use among current herbal remedies users	1/6 (16.6%)	0/2 (0%)	1/4 (25%)	1/4 (25%)	1/3 (33.3%)	0/1 (0%)	0/8 (0%)	0/8 (0%)	0/8 (0%)
Tobacco use among current herbal remedies non-users	13/94 (13.8%)	4/38 (3.6%)	9/56 (16.1%)	14/96 (14.6%)	11/67 (16.4%)	3/29 (10.3%)	60/240 (25%)	32/116 (27.6%)	28/124 (22.6%)

Table 8: Tobacco use among current herbal remedies users and non-users

Even if it is interesting to appreciate the similarity and, hence, the likely reliability of our findings in two series of patients recruited in separate hospitals, we consider the present study as preliminary, so that it is necessary further investigation to better assess the local and regional features of the use of herbal remedies both in different patients categories and in the general population.

	Cancer patients			Transplant patients			Other subjects		
	All	Males	Females	All	Males	Females	All	Males	Females
Alcohol use in current herbal remedies users	4/6 (66.6%)	1/2 (50%)	3/4 (75%)	1/4 (25%)	1/3 (33.3%)	0/1 (0%)	2/8 (25%)	0 (0%)	2/8 (25%)
Alcohol use in current herbal remedies non-users	20/94 (21.3%)	12/38 (31.6%)	8/56 (14.3%)	9/96 (9.3%)	8/67 (11.9%)	0/29 (0%)	29/280 (10.4)	23/116 (19.8%)	6/132 (4.5%)

**Table 9:** Alcohol use among current herbal remedies users and non-users

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