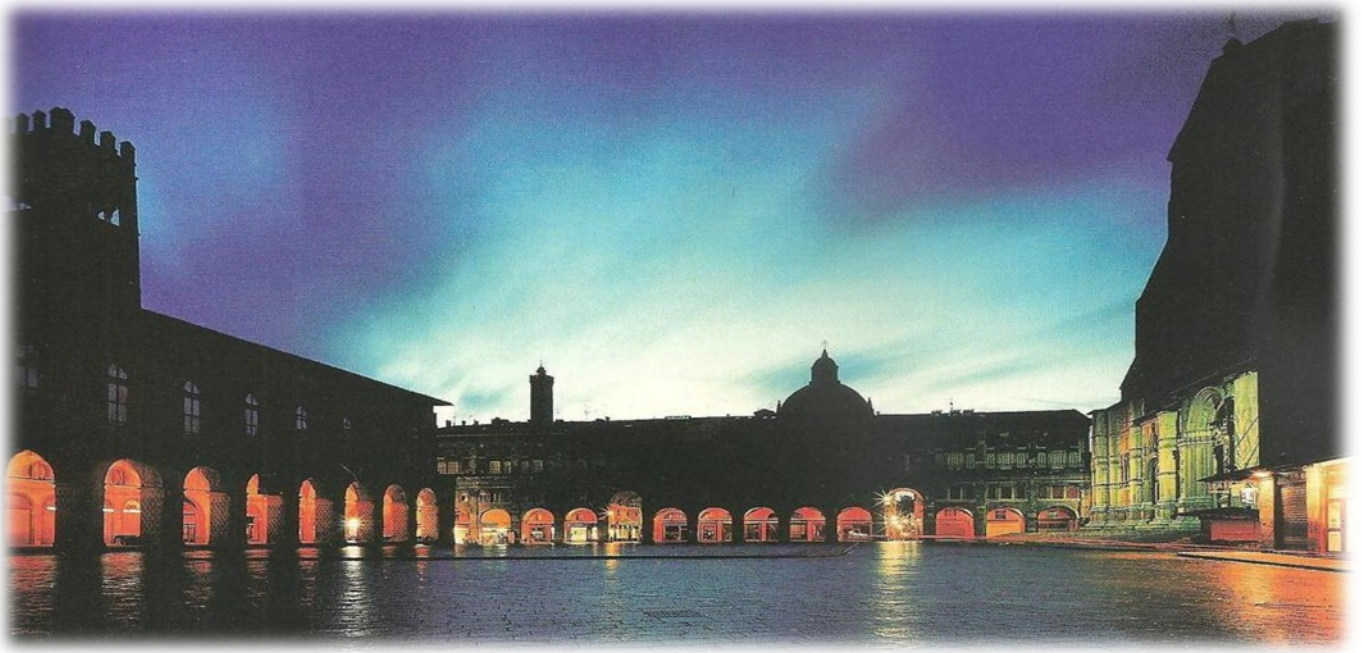
Dialogo sulle differenze tra Medicina Allopatica e Medicina Naturale: limiti e vantaggi delle due discipline



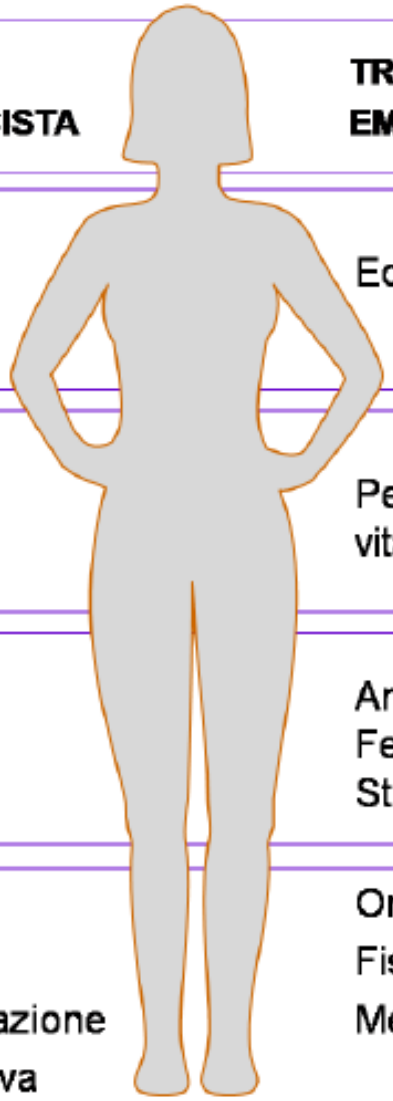
Dott. ER Cosentino

Dipartimento Cardio-Toraco-Vascolare

Università degli Studi di Bologna

La grande dicotomia del pensiero moderno

	TRADIZIONE RAZIONALISTA-MECCANICISTA	TRADIZIONE EMPIRICA-SISTEMICA
Concetto di salute	Normalità Assenza di sintomi	Equilibrio dinamico
Concetto di malattia	Anomalia di meccanismo (anatomico →molecolare)	Perturbazione della "forza vitale"
Metodi	Riduzionismo, analisi Esperimento Trials in doppio cieco	Analogia Fenomenologia Studi osservazionali
Terapie	Allopatia, chemioterapia Trapianti, chirurgia Ingegneria genetica, clonazione Terapia ormonale sostitutiva	Omeopatia Fisioterapia, psicoterapia Medicine orientali ed etniche



"La salute è il benessere fisico, mentale, sociale, non solo l'assenza di malattia"

O.M.S. 1974

Questa definizione, che ha il pregio di definire l' obiettivo (la salute è l'obiettivo di ogni terapia) in positivo, ed è per questo la miglior definizione allopatica di salute che possiamo trovare, rimane tuttavia troppo generica e quindi poco utile nel concreto.

Perché i pazienti usano le medicine non convenzionali?

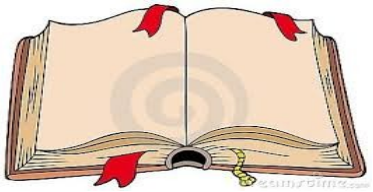
Motivazioni Positive

Fiducia nell'efficacia
Fiducia nella sicurezza
Ruolo attivo del paziente
Buon rapporto con il medico
Natura non invasiva
Accessibilità

Motivazioni Negative

Insoddisfazione per le cure convenzionali:
- -inefficacia per certe condizioni
- -effetti avversi
- -scarsa relazione medico paziente
- -liste di attesa

Rifiuto del sistema



E.Ernst, BMJ 200:321:1133-1134

EFFETTI COLLATERALI, 150MILA RICOVERI

Doctor-News 3 novembre 2004 - Anno 2, Numero 393

Ogni anno oltre 150 mila anziani vengono ricoverati in ospedale per gli effetti collaterali dei farmaci. Un dato allarmante anche perchè spesso i pazienti non superano la crisi.

- **-i farmaci assunti più frequentemente dagli anziani sono i:**
- **-i farmaci cardiovascolari (ace-inibitori: 33%, calcio antagonisti: 22.%),**
- **-l'aspirina a basse dosi (21%),**
- **-i farmaci contro i disturbi gastrointestinali (20%),**
- **-i farmaci per il sistema nervoso (17.%)**
- **-i farmaci contro i disturbi muscoloscheletrici (15%).**

Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study

Min Zhang, senior research fellow, C D'Arcy J Holman, professor of public health, Sylvie D Price, research associate, Frank M Sanfilippo, research fellow, David B Preen, senior research fellow, Max K Bulsara, associate professor of biostatistics

BMJ. 2009;338:a2752. doi: 10.1136/bmj.a2752.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Adverse drug reactions (ADRs) are a major public health problem in older populations

Repeat ADRs leading to hospital admission have increased at a greater rate than first time ADRs in older adults and by 2003 in Western Australia they had reached 30% of all ADRs

Little information is available on risk factors that predict repeat ADRs

WHAT THIS STUDY ADDS

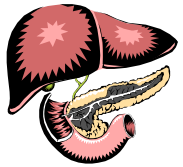
Comorbid congestive cardiac failure, diabetes, peripheral vascular, chronic pulmonary, hepatic, renal, rheumatological, and malignant diseases predict readmission for ADRs

Comorbid cerebrovascular disease, dementia, and paraplegia seem to protect against repeat ADRs, possibly because such patients are under closer healthcare supervision

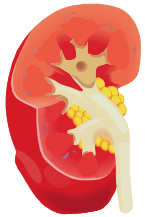
Alterazioni fisiologiche nell'anziano

Riduzione della motilità gastrica

Riduzione della secrezione acida/enzimatica

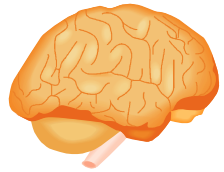


- Alterazione del numero di epatociti
- Riduzione produzione di albumina



- Riduzione numero glomeruli funzionanti
- Riduzione flusso ematico

- Alterazioni nella trasmissione neurochimica
- Riduzione capacità cognitive e dell'abilità



Mangoni AA, Jackson SH – Age-Related Changes in Pharmacokinetics: Basic Principals & Practical Applications. Br J Clin Pharmacol, 2004)

Eur J Clin Pharmacol (2013) 69:319–326
DOI 10.1007/s00228-012-1387-2

Sistema colinergico

- Diminuizione neuroni colinergici
- Diminuizione sintesi e rilascio di acetilcolina (Ach)
- Diminuizione densità dei recettori muscarinici

→ **Effetti anticolinergici centrali e periferici**

- **Interazioni:** Farmaco-Farmaco
  - Farmaco-Alimenti
  - Farmaco-Malattia
- Farmaco-prodotti da banco

Sistema adrenergico

- Diminuita produzione di AMPc
- Diminuizione densità dei recettori β
- Diminuita responsività dei recettori α_2

→ **Minore responsività dei barocettori**

Sistema dopaminergico

- Diminuizione neuroni colinergici
- Diminuizione sintesi e rilascio di acetilcolina (Ach)
- Diminuizione densità dei recettori muscarinici

→ **Effetti extrapiramidali**

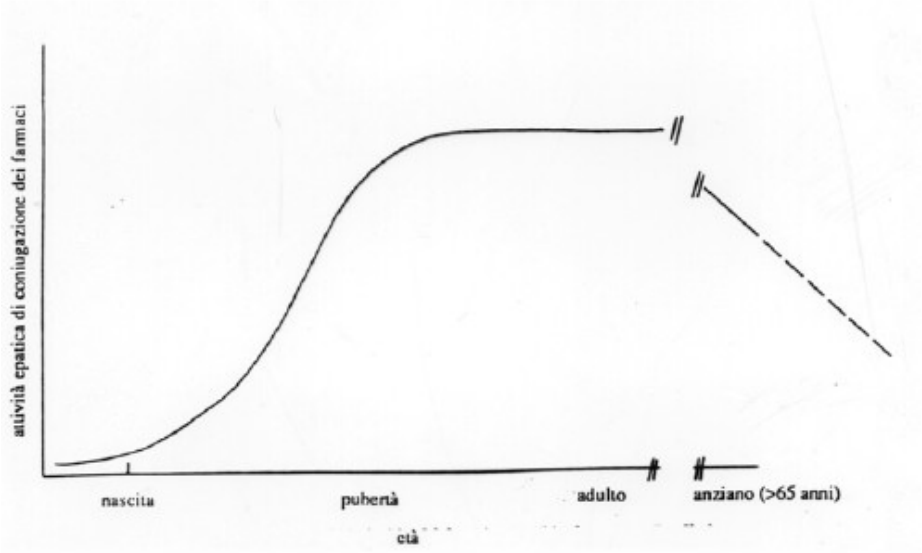
Polimorfismo genico CYP450 e PgP

Gareri & De Sarro, 2012

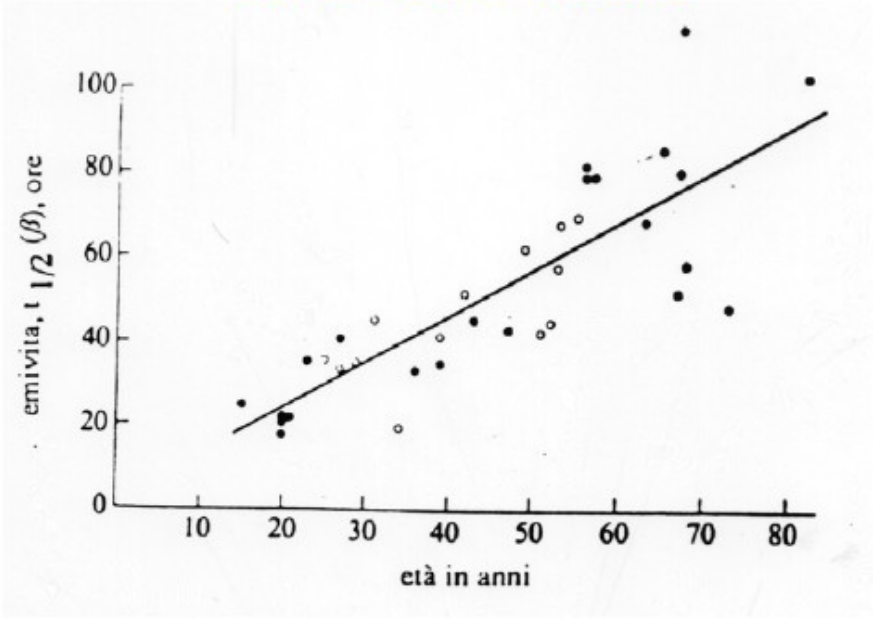
IL METABOLISMO DEI FARMACI DIPENDE DALL'ETA'

Durante l'arco della vita vi è una diversa capacità di metabolizzare i farmaci. L'attività metabolizzante del fegato è molto bassa alla nascita, cresce con l'età raggiungendo il massimo nell'adulto e diminuisce nell'anziano.

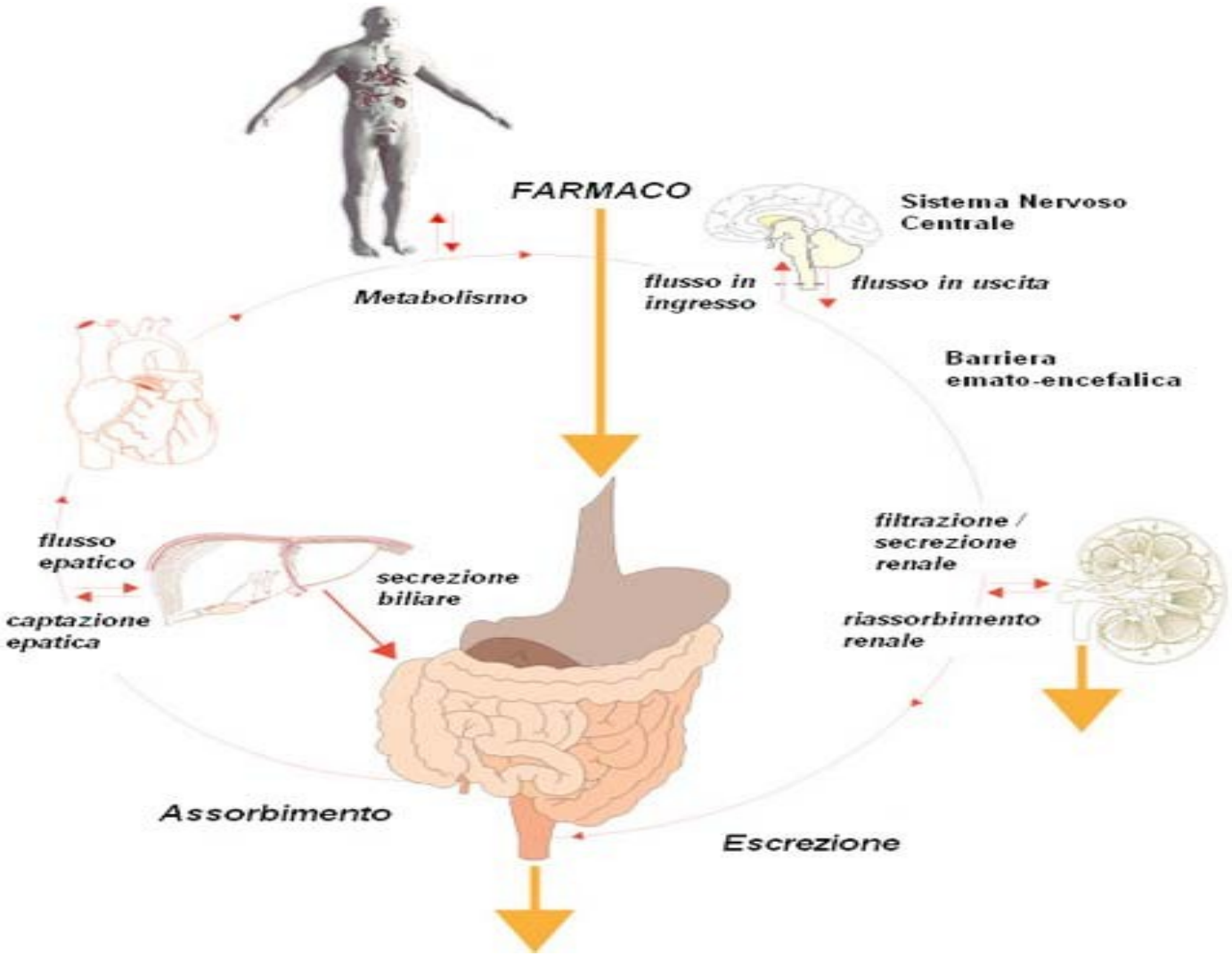
ONTOGENESI DEL METABOLISMO EPATICO



CORRELAZIONE TRA METABOLISMO DEL DIAZEPAM ED ETA'

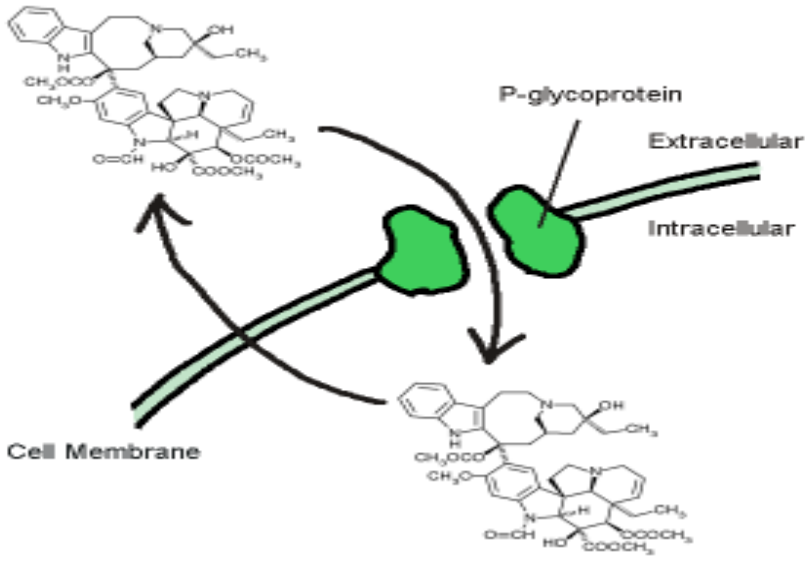


Fattori che influenzano la distribuzione dei farmaci



Legame alle proteine

- Mentre la prima lega i farmaci acidi, l'α 1-glicoproteina acida e le lipoproteine legano preferenzialmente i farmaci basici. Anche nell'anziano la distribuzione dei farmaci è soggetta a modificazioni: nell'organismo è documentabile una riduzione dei livelli di albumina ed un aumento dell'α-1-glicoproteina acida.
- Questo può causare un aumento significativo della frazione libera



Farmacovigilanza di genere

Le reazioni avverse sono più frequenti nel sesso femminile: circa 2 volte in più rispetto ai maschi (dati ISTAT).

In uno studio multicentrico di farmacovigilanza intensiva si è utilizzata un' analisi statistica specifica per criteri come età, indice di massa corporea e numero di farmaci prescritti contemporaneamente.

Si è così dimostrata una influenza significativa del sesso femminile per le reazioni avverse, specie se dose correlata, con una costante correlazione (presente anche nel maschio) per il numero di farmaci correntemente assunti.

Perché Farmacovigilanza in Pediatria?

Molti Clinical Trials non includono i pazienti minori di 18 anni o non includono pazienti pediatrici di varie fasce d'età

- Al momento dell'immissione in commercio di un farmaco non sono disponibili dati di sicurezza nella popolazione pediatrica (50%-70% dei farmaci non appositamente autorizzato e studiato per i bambini)

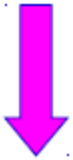
- Esiste una certa riluttanza ad includere soggetti pediatrici nei trial clinici per non creare alcun tipo di sofferenza o disagio (Pregiudizio etico, costo dei trial clinici)

Di conseguenza, molti farmaci sono prescritti ai bambini

"off-label"

Perché Farmacovigilanza in Pediatria?

L'uso off-label di farmaci pediatrici varia tra il 18-65% delle prescrizioni ospedaliere e tra l'11% ed il 31% nell'assistenza primaria



La mancanza di dati sulla sicurezza d'impiego può incrementare il rischio di ADR

Errori in terapia

Il 30% degli errori di terapia riportati ai centri antiveleni negli USA ha coinvolto bambini < 6 anni

- Pochi studi hanno esaminato gli errori di terapia al di fuori del setting assistenziale ospedaliero

Studi su errori associati all'health litteracy

Studi sull'inappropriatezza dei device utilizzati per la somministrazione

Studi su variabilità dell'etichettatura e confezionamento dei farmaci

Out-of-Hospital Medication Errors Among Young Children in the United States, 2002–2012

AUTHORS: Maxwell D. Smith,[a] Henry A. Spiller, MS, D.ABAT,[b,c] Marcel J. Casavant, MD,[b,c] Thiphalak Chounthirath, MS,[a] Todd J. Brophy, BS,[a,c] and Huiyun Xiang, MD, MPH, PhD[a,c]

Obiettivo:

Valutare errori di terapia tra i bambini < 6 anni negli usa presenti nel National Poison Database System dal 2002 al 2012.

Risultati:

- 696.937 errori di terapia segnalati in bambini < 6 anni (1 bambino ogni 8 minuti!)
- Il tasso di segnalazione è più alto per i bambini < 1 anno (25% segnalazioni)
- Il maggior numero delle segnalazioni coinvolgeva le formulazioni liquide

TABLE 2 Characteristics of Route of Exposure and Type of Medication Error by Child Age, NPDS 2002–2012

Characteristics	Age, y							Total
	<1	1	2	3	4	5	<6[a]	
Route of exposure								
Ingestion	167 530	138 558	121 538	96 437	79 796	64 927	1529	670 315 (96.2)
Ocular	2267	1942	1467	1084	1014	925	62	8761 (1.3)
Inhalation/nasal	2737	1157	974	920	867	843	22	7520 (1.1)
Rectal	502	551	495	332	210	116	10	2216 (0.3)
Two or more routes	412	275	363	297	290	275	6	1918 (0.3)
Parenteral	689	326	223	165	223	217	23	1866 (0.3)
Otic	334	504	344	239	208	164	21	1814 (0.3)
Dermal	545	391	286	222	163	163	11	1781 (0.3)
Vaginal	18	25	36	25	23	13	3	143 (0.0)
Aspiration (with ingestion)	14	7	6	3	0	0	0	30 (0.0)
Other	235	75	64	49	33	43	3	502 (0.1)
Unknown/Missing[b]	16	13	11	9	12	8	2	71
Type of medication error								
Inadvertently took/given medication twice	38 426	38 658	36 912	29 414	24 732	19 837	420	188 399 (27.0)
Confused units of measure	16 019	12 018	9963	7987	6507	4795	100	57 389 (8.2)
Wrong medication taken/given	14 862	11 012	8831	7153	6331	6208	96	54 493 (7.8)
Medication doses given/taken too close together	12 745	10 873	8074	6300	5329	4245	144	47 710 (6.8)
Inadvertently took/given someone else's medication	8830	9249	9424	7298	6422	6256	55	47 534 (6.8)
Dispensing cup error	9074	7383	6270	5112	4067	3095	46	35 047 (5.0)
Other/unknown therapeutic error	9135	6743	5972	4868	3841	3148	149	33 856 (4.9)
Incorrect formulation or concentration given	9395	7565	5600	4319	3298	2497	71	32 745 (4.7)
Two or more errors	8392	5561	4532	3578	3139	2849	87	28 138 (4.0)
More than 1 product containing same ingredient	1328	2586	2984	2565	2253	1873	33	13 622 (2.0)

Esiste una alternativa alla medicina tradizionale?

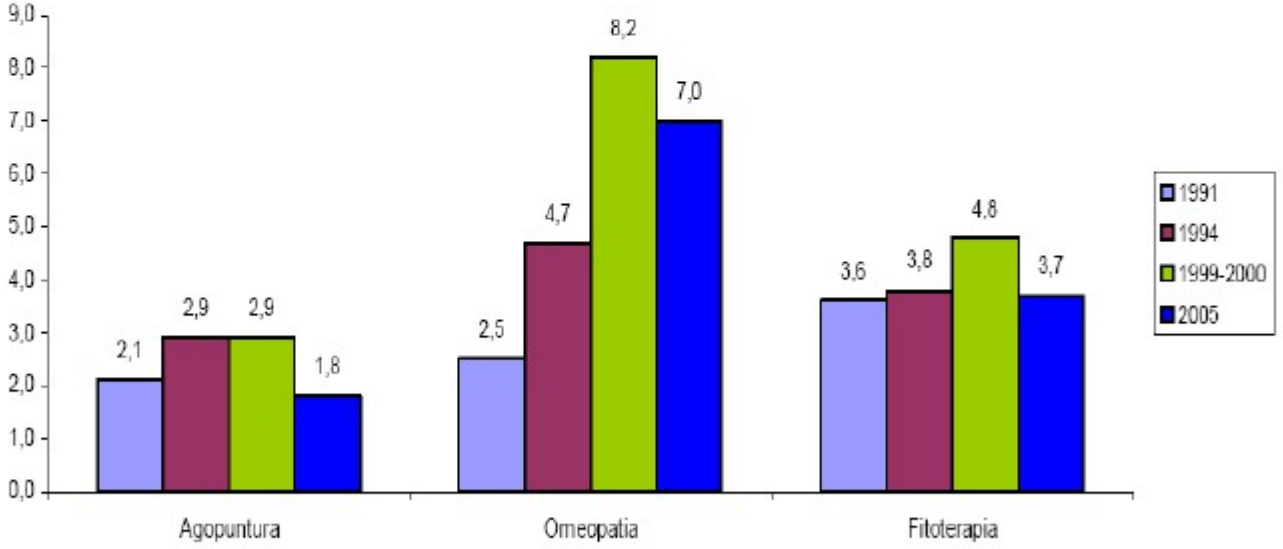
DATI ISTAT 2007

sanità

Istituto nazionale di statistica

STATISTICHE IN BREVE

Grafico 2 - Persone che nei 3 anni precedenti l'intervista hanno fatto uso di agopuntura, omeopatia, fitoterapia - Anni 1991 ,1994, 1999 - 2000, 2005 (per 100 persone)



Istat

L'OMEOPATIA NEL MONDO

- DIFFUSIONE IN PERCENTUALE
  - 70% in Europa (Francia – Germania – Italia – Paesi Bassi)
  - 30% nel resto del Mondo (India – Brasile – U.S.A. – ecc.)
- MEDICI PRESCRITTORI DI MEDICINALI OMEOPATICI: 200.000
- PAZIENTI CHE USUFRUISCONO DELLA MEDICINA OMEOPATICA: 200 milioni
- FATTURATO INDUSTRIA OMEOPATICA: 1 miliardo di Euro
- PERCENTUALE DEL MERCATO DEL FARMACO: 0,5% circa

MEDICINA OMEOPATICA

L'Omeopatia è un metodo clinico terapeutico basato sulla "**LEGGE DEI SIMILI**" formulata per la prima volta da **IPPOCRATE** (460-370 a.C.)

e sistematizzata da **C.S.HAHNEMANN** (1755-1843), tramite l'utilizzo in "**DOSI INFINITESIMALI**" di sostanze di origine vegetale, minerale o animale a diverse deconcentrazioni o diluizioni che a dosi tossiche o subtossiche provocano nell'uomo sano sintomi analoghi a quelli riscontrabili nel malato in esame

La farmacologia omeopatica classica
- **MATERIA MEDICA** -
è costituita da una serie di medicinali tratti dal mondo:

MINERALE

VEGETALE

ANIMALE

Nel 1984 il francese **AUBIN** ha verificato tale legge studiando l'azione dell'**ACONITINA** sul cuore isolato di anguilla : ha constatato che con concentrazioni di Aconitina di 1 X 10-5 M si ha tachicardia, mentre per concentrazioni di Aconitina di 1 X 10-7 M si ottiene un effetto bradicardico

- **ACONITINA 1 X 10^{-5}** → **TACHICARDIA**
- **ACONITINA 1 X 10^{-7}** → **BRADICARDIA**
- **ACONITINA 1 X 10 -18** → **Nessun effetto sul cuore sano ma normalizzazione del ritmo sul cuore preintossicato**

(Necessità della sensibilizzazione)

Homeopathic medicines for children

M Erlewyn-Lajeunesse

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Published Online First
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ABSTRACT
This article describes the homeopathic tradition and considers the safety, manufacture, effectiveness and regulation of homeopathic medicines. These medicines are commonly purchased without prescription for children, so an understanding of the basis of therapy is important to ensure appropriate and safe usage. The role of integrated medicine in the National Health Service is also reviewed with identification of research priorities.

Homeopathy is a form of complementary and alternative medicine (CAM). In 2007 it supported an industry worth £37 million in the UK (US$62 million), a relatively small amount in view of its popularity in France, Germany and Italy.[1 2] Many families purchase homeopathy products as self-help remedies over the counter in pharmacies. Homeopathic products are used in this way by 10–18% of parents to treat minor paediatric self-limiting conditions such as teething, bruises and colic.[3 4] Use in allergic diseases such as eczema and asthma may be considerably higher.[5 6] Homeopathy is used in preschool children to complement allopathic medicines; its use is associated with higher maternal education, other CAM usage and childhood allergies.[7] Among general practitioners, homeopathic prescribing is highest in children under 12 months of age.[8 9] Despite its popularity, up to two-thirds of parents will not disclose CAM use to their doctors[10] as they consider that their doctors do not need to know.[11] Direct questions about the use of CAM therapy when taking a history reveal not only what therapies have been accessed, but also why these therapies have been sought.

WHAT IS HOMEOPATHY?

Homeopathy is a traditional form of medicine underpinned by two basic principles. First, homeopaths select remedies using the principle of 'like treats like'.[12] Samuel Hahnemann, a German doctor (1745–1843), discovered this maxim while experimenting on himself. He noticed that consumption of the bark of the Peruvian Cinchona tree induced malaria-like symptoms and concluded that substances that replicate symptoms could be used to treat the disease that caused the original symptoms (Hahnemann was probably suffering from cinchonism caused by quinine in the bark). Despite his failure to understand the mechanisms at work, homeopathy has been based on the principle of like treats like ever since. Many fundamental scientific discoveries are based on luck rather than judgement: Sir Alexander Fleming's discovery of penicillin was similarly fortuitous.[13] If necessity is the mother or invention, perhaps serendipity is its father.

Second, homeopathic remedies are believed to gain greater potency as they are diluted. Reducing the toxicity of 18th century herbal and mineral concoctions was probably a sensible idea and was not controversial at the time. However, remedies are diluted to a degree where they are unlikely to contain any of the original substance. All modern scientifically trained practitioners find this lack of biological plausibility particularly difficult, and it has been used to criticise homeopathy.

REMEDIES

Homeopathic remedies are based on a mother tincture created by dissolving material in water or alcohol. Materials used include inert minerals, chemicals, drugs and biological matter from bacteria, viruses, plants, animals and human tissue or secretions. Some homeopaths use remedies based upon imponderabilia from electromagnetic radiation such as the remedy Sol from sunlight. The majority of commonly prescribed remedies are based on plants or minerals (table 1).[9]

Homeopathic practice relies on clinical observation and has built up complex constellations of symptoms and signs that have become associated with particular remedies. Extremely few of these clinical pictures are recognised in allopathic medicine, yet they can be observed by careful clinical assessment, and as such form part of the human condition. Such is the complexity of homeopathic prescribing that a cross-referencing repertory is often required to match symptoms to their remedies. These references have benefited from computerisation, and repertory programmes are in common use.[14]

POTENCY AND DILUTION

The more dilute a homeopathic remedy, the more potent it is considered to be. The dilution process involves vigorous shaking ('sucussion') of the preparation between dilutions as this is believed to 'potentise' the mixture by extracting a vital force from the substance. Dilution is performed in decimal (1:10) or centesimal (1:100) steps, using a multiple phial (Hahnemanian) or a single phial technique (Korsakovian).

The single phial method is quicker but less accurate. The phial is filled with 100 parts mother tincture and then emptied; the remnant of the tincture held by capillary attraction to the side of phial is subsequently diluted with 99 parts water, leading to an approximate centesimal dilution, which is then repeated to the desired potency. Homeopathic remedies are labelled according to the number of stages of dilution, using either decimal (X or D) or centesimal methods (Hahnemanian (C) or Korsakovian (K)). Thus a 6X potency is diluted through six sequential decimal

International Seminars in Surgical Oncology

Published: 30 April 2007

International Seminars in Surgical Oncology 2007, **4**:10 doi:10.1186/1477-7800-4-10

Review

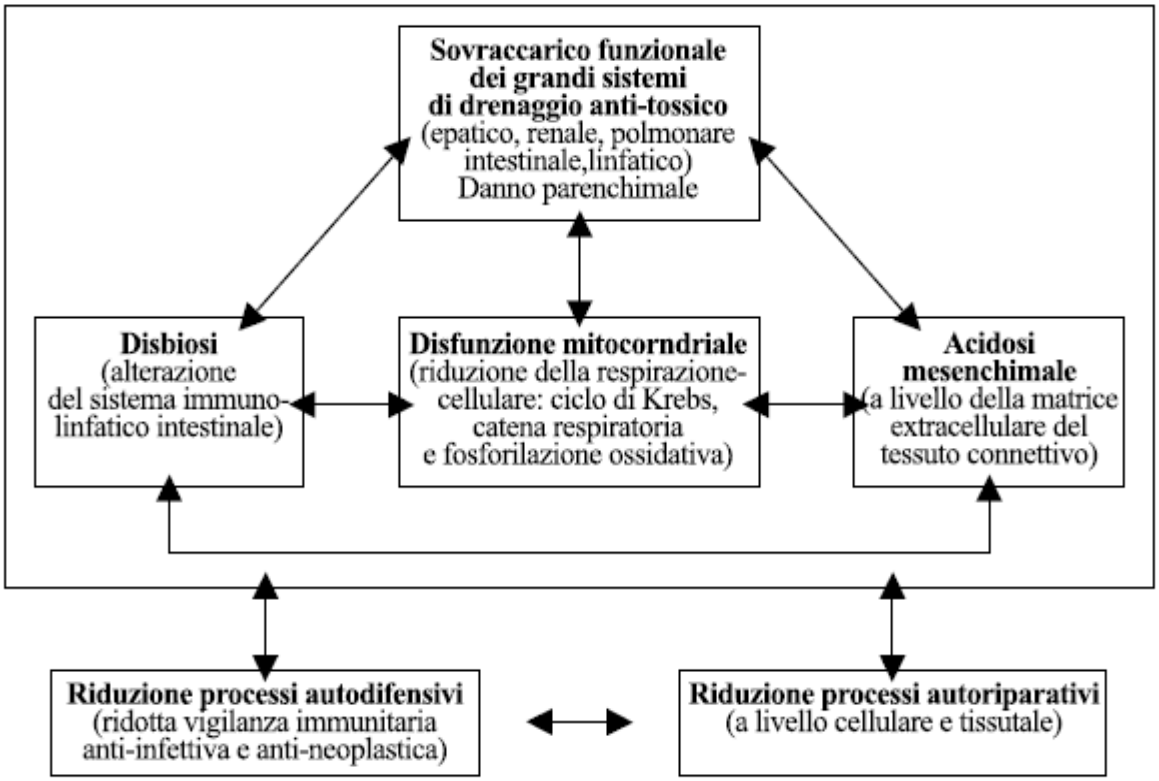
Open Access

The use of complementary and alternative medicine by cancer patients

Mariama Adams* and Andrew Paul Jewell

Abstract

The use of Complementary and Alternative Medicine (CAM) among cancer patients is widespread and appears to be increasing. However, it is not clear whether patients use CAM as an 'alternative' to standard oncology care or as an adjunct to the conventional treatment they receive. This study reviews the role of CAM therapies in the management of cancer, from the view of both patients and health professionals and it highlights issues relating to the efficacy of CAM used by cancer patients. Most patients use CAM to 'complement' the conventional therapies of radiotherapy, chemotherapy, hormone therapy and surgery. Health professionals in general have expressed positive views when CAM is used 'complementarily' and not as an 'Alternative'. Results so far published have shown that CAM can contribute to improving the quality of life of cancer patients and their general well-being.



Le alterazioni indotte dalla chemioterapia nella rete dei processi autopoietici

DOI:10.1093/jncimonographs/lgu041

Clinical Practice Guidelines on the Use of Integrative Therapies as Supportive Care in Patients Treated for Breast Cancer

Heather Greenlee, Lynda G. Balneaves, Linda E. Carlson, Misha Cohen, Gary Deng, Dawn Hershman, Matthew Mumber, Jane Perlmutter, Dugald Seely, Ananda Sen, Suzanna M. Zick, Debu Tripathy; for the Society for Integrative Oncology Guidelines Working Group

Correspondence to: Heather Greenlee, ND, PhD, MPH, Department of Epidemiology, Mailman School of Public Health, Columbia University, 722W. 168th Street, 7th Floor, New York, NY 10032 (e-mail: hg2120@columbia.edu).

Background The majority of breast cancer patients use complementary and/or integrative therapies during and beyond cancer treatment to manage symptoms, prevent toxicities, and improve quality of life. Practice guidelines are needed to inform clinicians and patients about safe and effective therapies.

Methods Following the Institute of Medicine's guideline development process, a systematic review identified randomized controlled trials testing the use of integrative therapies for supportive care in patients receiving breast cancer treatment. Trials were included if the majority of participants had breast cancer and/or breast cancer patient results were reported separately, and outcomes were clinically relevant. Recommendations were organized by outcome and graded based upon a modified version of the US Preventive Services Task Force grading system.

Results The search (January 1, 1990–December 31, 2013) identified 4900 articles, of which 203 were eligible for analysis. Meditation, yoga, and relaxation with imagery are recommended for routine use for common conditions, including anxiety and mood disorders (Grade A). Stress management, yoga, massage, music therapy, energy conservation, and meditation are recommended for stress reduction, anxiety, depression, fatigue, and quality of life (Grade B). Many interventions ($n = 32$) had weaker evidence of benefit (Grade C). Some interventions ($n = 7$) were deemed unlikely to provide any benefit (Grade D). Notably, only one intervention, acetyl-L-carnitine for the prevention of taxane-induced neuropathy, was identified as likely harmful (Grade H) as it was found to increase neuropathy. The majority of intervention/modality combinations ($n = 138$) did not have sufficient evidence to form specific recommendations (Grade I).

Conclusions Specific integrative therapies can be recommended as evidence-based supportive care options during breast cancer treatment. Most integrative therapies require further investigation via well-designed controlled trials with meaningful outcomes.

J Natl Cancer Inst Monogr 2014;50:346–358

Rationale and Importance

(ie, vitamins, minerals, botanicals, and fish oil) and mind-body

Clinical applications	Recommendations	Strength of evidence
Anxiety/stress reduction	Music therapy is recommended for reducing anxiety during RT and CT sessions	B
	Meditation is recommended for reducing anxiety in BC patients and those undergoing RT	B
	Stress management is recommended for reducing anxiety during treatment, but longer group programs are likely better than self-administered home programs or shorter programs	B
	Yoga is recommended for reducing anxiety in BC patients undergoing RT +/– CT and suggested for fatigued patients	B
	Acupuncture can be considered for reducing anxiety in fatigued BC patients	C
	Massage can be considered for short-term reduction of anxiety in BC patients	C
	Relaxation can be considered for treating anxiety during treatment	C
Depression/mood	Meditation, particularly MBSR, is recommended for treating mood disturbance and depressive symptoms in BC patients undergoing RT	A
	Relaxation is recommended for improving mood and depressive symptoms when added to SC	A
	Yoga is recommended for improving mood in women undergoing RT +/– CT and for fatigued BC patients in addition to SC	A
	Massage is recommended for improving mood disturbance in posttreatment BC patients	B
	Music therapy is recommended for improving mood in newly diagnosed BC patients	B
	Acupuncture can be considered for improving mood in postmenopausal women experiencing hot flashes or fatigue	C
	Healing touch can be considered for improving mood in BC patients undergoing CT	C
	Stress management interventions with or without exercise can be considered for improving mood in BC patients	C

Fatigue	Energy conservation counseling is recommended for the treatment of fatigue	B
	American ginseng can be considered as an herbal approach for the treatment of fatigue in BC patients	C
	Acupuncture can be considered for the treatment of fatigue after the completion of cancer treatments	C
	Modified qigong can be considered for the treatment of fatigue in BC patients	C
	Acetyl-L-carnitine is not recommended for the treatment of fatigue due to lack of effect	D
	Guarana is not recommended as an herbal for the treatment of fatigue due to lack of effect	D
Sleep	Stress management techniques can be considered for the treatment of sleep disruption	C
	Gentle yoga can be considered for the treatment of sleep disruption	C
Quality of life and physical functioning	Meditation is recommended for improving quality of life among BC patients	A
	Acupuncture can be considered for improving quality of life among cancer patients	C
	Guided imagery can be considered for improving quality of life among BC patients	C
	Mistletoe can be considered for improving quality of life among BC patients	C
	Qigong can be considered for improving quality of life in cancer patients	C
	Reflexology can be considered for improving quality of life among BC patients	C
	Stress management can be considered for improving quality of life among BC patients	C
	Yoga can be considered for improving quality of life among BC patients	C
	Exercise/awareness can be considered for improving functioning among BC patients	C
	Energy conservation is not recommended for improving functioning among BC cancer patients due to lack of effect	D
CINV	Acupressure can be considered for BC patients receiving CT as an addition to antiemetics to help control nausea and vomiting during CT	B
	Electroacupuncture can be considered for BC patients as an addition to antiemetics to control vomiting during CT	B
	Ginger can be considered for BC patients receiving CT, without concurrent RT as an addition to antiemetics for the control of acute nausea	C
	PMR can be considered for BC patients receiving CT as an addition to antiemetics to help control nausea and vomiting during CT	C
	Glutamine is not recommended for use by BC patients receiving CT for the treatment of CINV due to lack of effect	D

OMEOPATIA e FITOTERAPIA

- **Uno degli equivoci più diffusi è quello di confondere l'omeopatia con la fitoterapia e di considerare l'omeopata come una specie di "super-erborista".**

REVIEW Open Access

Pharmacological effects of *Radix Angelica Sinensis* (*Danggui*) on cerebral infarction

Yi-Chian Wu[1] and Ching-Liang Hsieh[1,2,3*]

Abstract

Radix Angelica Sinensis, the dried root of *Angelica sinensis* (*Danggui*), is a herb used in Chinese medicine to enrich blood, promote blood circulation and modulate the immune system. It is also used to treat chronic constipation of the elderly and debilitated as well as menstrual disorders. Research has demonstrated that *Danggui* and its active ingredients, as anti-arthrosclerotic, anti-hypertensive, antioxidant anti-inflammatory agents which would limit platelet aggregation, are effective in reducing the size of cerebral infarction and improving neurological deficit scores.

Table 1 Possible pharmacological actions of *Radix Angelica Sinensis* on cerebral infarction

Pharmacological actions	Related components	Possible mechanisms
Anti-arthrosclerosis effects	*Danggui* and sodium ferulate	reverse the reduction of TGB-β/reverse the increase of bFGF [24]
	Danggui	reduce the increase of serum malonyldialdehyde (MDA) levels [25]
	sodium ferulated	decrease the levels of triglyceride [11]
Vasodilatation and improving microcirculation effects	*Danggui*	increase the formation of NO and mediate the inhibition of calcium influx [10]
	sodium ferulate	increase the generation of NO [11]
	Ligustilide	inhibit prostaglandin F-2α, oxytocin, acetylcholine chloride, and potassium depolarization-induced muscle contraction [12]
	Ligustilide	increase the number of opened capillary and the speed of blood flow [13]
	Ferulic acid	enhance acetylcholine-induced vasodilatation and reduce the production of thromboxane B_2 [14]
Anti-platelet aggregation effects	*Danggui* and sodium ferulate	inhibit ADP-induced and collagen-induced platelet aggregation [27]
	Z-Ligustilide	inhibit ADP-induced platelet aggregation [28]
Anti-inflammatory effects	Ferulic acid	inhibit ICAM-1 and NF-κB expression [33]
	Ferulic acid	enhance gamma-aminobutyric acid type B1 ($GABA_{B1}$) receptor expression [34]
	Danggui	reduce TNF-α and TGF-ß1 mRNA expression [35]
	Danggui polysaccharides	reduce TNF-α levels [36]
Anti-oxidative effects	Ferulic acid	reduce the generation of NADPH-dependent production of superoxide anion [14]
	Ferulic acid	enhances the expression of $GABA_{B1}$ receptor expression [34]
	Z-ligustilide	reduce MDA levels and increase GSH-PX and SOD activities [42]

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Communication

Anti-Osteoporotic Effects of *Angelica sinensis* (Oliv.) Diels Extract on Ovariectomized Rats and Its Oral Toxicity in Rats

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Abstract: *Angelica sinensis* root is one of the herbs most commonly used in China; it is also often included in dietary supplements for menopause in Europe and North America. In the present study, we examined the anti-osteoporotic effects of *A. sinensis* extract in an ovariectomized (OVX) rat model of osteoporosis as well as toxicity of the extract after repeated oral administration. The OVX rats were treated with 17β-estradiol (10 μg/kg i.p. once daily) or *A. sinensis* extract (30, 100, and 300 mg/kg, p.o. once daily) for four weeks. The bone (femur) mineral density (BMD) of rats treated with the extract (300 mg/kg) was significantly higher than that of the OVX-control, reaching BMD of the estradiol group. Markers of bone turnover in osteoporosis, serum alkaline phosphatase, collagen type I C-telopeptide and osteocalcin, were significantly decreased in the extract group. The body and uterus weight and serum estradiol concentration were not affected, and no treatment-related toxicity was observed during extract administration in rats. The results obtained indicate that *A. sinensis* extract can prevent the OVX-induced bone loss in rats via estrogen-independent mechanism.

Keywords: *Angelica sinensis* root; oral toxicity; osteoporosis; ovariectomized

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Risks and Benefits of Commonly used Herbal Medicines in México

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Abstract

In Mexico, local empirical knowledge about medicinal properties of plants is the basis for their use as home remedies. It is generally accepted by many people in Mexico and elsewhere in the world that beneficial medicinal effects can be obtained by ingesting plant products. In this review, we focus on the potential pharmacologic bases for herbal plant efficacy, but we also raise concerns about the safety of these agents, which have not been fully assessed. Although numerous randomized clinical trials of herbal medicines have been published and systematic reviews and meta-analyses of these studies are available, generalizations about the efficacy and safety of herbal medicines are clearly not possible. Recent publications have also highlighted the unintended consequences of herbal product use, including morbidity and mortality. It has been found that many phytochemicals have pharmacokinetic or pharmacodynamic interactions with drugs. The present review is limited to some herbal medicine that are native or cultivated in Mexico and that have significant use. We discuss the cultural uses, phytochemistry, pharmacological and toxicological properties of the following following plant species: Nopal (*Opuntia ficus*), Peppermint (*Mentha piperita*), Chaparral (*Larrea divaricata*), Dandlion (*Taraxacum officinale*), Mullein (*Verbascum densiflorum*), Chamomile (*Matricaria recutita*), Nettle or Stinging Nettle (*Urtica dioica*), Passionflower (*Passiflora incarmata*), Linden Flower (*Tilia europea*), and Aloa (*Aloa vera*). We conclude that our knowledge of the therapeutic benefits and risks of some herbal medicines used in Mexico is still limited and efforts to elucidate them should be intensified.

Chamomile (*Matricaria recutita*)

Chamomile (*Matricaria recutita*) is one of the most popular single ingredient herbal teas, or tisanes. Chamomile tea, brewed from dried flower heads is used traditionally for several medicinal purposes as Gastrointestinal tract ailments as flatulence, nervous diarrhea, spasms, colitis, gastritis, and hemorrhoids. Other uses include nasal mucous membrane inflammation, allergic rhinitis, attention deficit-hyperactivity disorder (ADHD), restlessness, insomnia, dysmenorrhea, mastitis, and varicose ulcers (See Table1). Chamomile contains quercetin, apigenin, coumarins, and the essential oils matricin, chamazulene, alpha bisaboloid, and bisaboloid oxides (Szoke et al., 2004).

Clinical studies have shown that chamomile might be effective for the treatment of dyspepsia and mucositis. Preliminary research suggests that it blocks slow wave activity in the small intestine, which could slow peristaltic movement (Melzer et al., 2004). In a clinical trial of 98 patients receiving local radiation and systemic chemotherapy, chamomile oral rinse prevented mucositis secondary to radiation therapy and some types of chemotherapeutic drugs including asparaginase, cisplatin, cyclophosphamide, daunorubicin, doxorubicin, etoposide, hydroxyurea, mercaptopurine, methotrexate, procarbazine, and vincristine (McKay and Blumberg, 2006). Chamomilla contains flavonoids, which exert benzodiazepine-like activity (Avallone et al., 2000), and also has a phosphodiesterase inhibitory action, which leads to increased cAMP levels (Kuppusamy and Das, 1992). Gomaa et al. (2003) reported the effect of flavonoids present in chamomilla on inhibition of morphine withdrawal *in vitro*. Recently, Kassi et al., (2004) demonstrated that aqueous extracts of chamomile induce osteoblast differentiation and have anti-cancer effects on breast cancer and uterine cancer *cells in vitro* (concentrations of 10-100 μg/mL). They concluded that chamomile extracts produce these effects because it acts as selective estrogen receptor modulator.

Several reports have appeared in the literature about the toxic effects of chamomile. It has been observed that orally chamomile tea can cause allergic reactions including severe hypersensitivity reactions and anaphylaxis in sensitive individuals (Paulsen, 2002). Chamomile tea can also cause an allergic conjunctivitis. Cases of contact dermatitis (but not reactions of type I) were reported following its topical applications (De Smet, 2002; Federici et al., 2005).

It has been suggested that there are important interactions between chamomile and conventional drugs. Although no evidence of a drug–herb interaction between warfarin and chamomile has been documented, there is a theoretical risk because chamomile contains coumarins. Segal and Pilote (2006) have documented a case of a 70-year-old woman who, while being treated with warfarin, was admitted to hospital with multiple internal hemorrhages after having used chamomile products (tea and body lotion) to soothe upper respiratory tract symptoms. Ganzera et al., (2006) have studied the effect of chamomile essential oil and its major constituents on four selected human cytochrome P450 enzymes (CYP1A2, CYP2C9, CYP2D6 and CYP3A4) *in vitro*. Crude essential oil showed inhibition of each of the enzymes, with CYP1A2 being more sensitive than the other isoforms. Three constituents of the oil,

Grapefruit juice: potential drug interactions

Reason for posting: Grapefruit juice interacts with a number of medications. This unusual discovery was made serendipitously in 1989 during an experiment designed to test the effect of ethanol on a calcium-channel blocker.[1] The observed response was later determined to be due to the grapefruit juice delivery vehicle rather than the alcohol. In the past decade, the list of drug interactions with grapefruit juice has expanded to include several classes of medication, precipitating a recent advisory from Health Canada.[2]

The interaction: As little as 250 mL of grapefruit juice can change the metabolism of some drugs.[3] This drug–food interaction occurs because of a common pathway involving a specific isoform of cytochrome P450 — CYP3A4 — present in both the liver and the intestinal wall. Studies suggest that grapefruit juice exerts its effect primarily at the level of the intestine.[4]

After ingestion, a substrate contained in the grapefruit binds to the intestinal isoenzyme, impairing first-pass metabolism directly and causing a sustained decrease in CYP3A4 protein expression.[5] Within 4 hours of ingestion, a reduction in the effective CYP3A4 concentration occurs, with effects lasting up to 24 hours.[6] The net result is inhibition of drug metabolism in the intestine and increased oral bioavailability. Because of the prolonged response, separating the intake of the drug and the juice does not prevent interference.

Individuals express CYP3A4 in different proportions, those with the highest intestinal concentration being most susceptible to grapefruit juice–drug interactions.[5] An effect is seen with the whole fruit as well as its juice, so caution should be exercised with both.[7] The precise chemical compound in grapefruit that causes the interaction has not been identified. There is no similar reaction with orange juice, although there is some suspicion that "sour oranges" such as the Seville variety, may have some effect.[8] A recent study, however, that tested the known interference of grapefruit juice with cyclosporine showed no similar effect with Seville oranges.[9]

There is some interest in the potential therapeutic benefit of adding grapefruit juice to a drug regimen to increase oral bioavailability.[3] The limitation is the individual variation in patient response. However, if the chemical that causes grapefruit's CYP3A4 inhibition is elucidated, there may be an opportunity to modulate that pathway in a controlled fashion.

Phenotyping Studies to Assess the Effects of Phytopharmaceuticals on *In Vivo* Activity of Main Human Cytochrome P450 Enzymes

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Key words
- cytochrome P450
- cocktail interaction studies
- herb-drug interaction
- phytopharmaceuticals
- botanicals
- herbal products

Abstract

The extensive use of herbal drugs and their multiple components and modes of action suggests that they may also cause drug interactions by changing the activity of human cytochrome P450 enzymes. The purpose of the present review is to present the available data for the top 14 herbal drug sales in the U.S. Studies describing the effects of herbal drugs on phenotyping substrates for individual CYPs were identified by a comprehensive MEDLINE search. Drugs included *Allium sativum* (Liliaceae), *Echinacea purpurea* (Asteraceae), *Serenoa repens* (Arecaceae), *Ginkgo biloba* (Ginkgoaceae), *Vaccinium macrocarpon* (Ericaceae), *Glycine max* (Fabaceae), *Panax ginseng* (Araliaceae), *Actea racemosa* (Ranunculaceae), *Hypericum perforatum* (Hypericaceae), *Silybum marianum* (Asteraceae), *Camellia sinensis* (Theaceae), *Valeriana officinalis* (Valerianaceae), *Piper methysticum* (Piperaceae), and *Hydrastis canadensis* (Ranunculaceae) preparations. We identified 70 clinical studies in 69 publications. The majority of the herbal drugs appeared to have no clear effects on most of the CYPs examined. If there was an effect, there was mild inhibition in almost all cases, as seen with garlic or kava effects on CYP2E1 and with soybean components on CYP1A2. The most pronounced effects were induction of CYP3A and other CYPs by St. John's wort and the inhibitory effect of goldenseal on CYP3A and CYP2D6, both being borderline between mild and moderate in magnitude. With the exceptions of St. John's wort and goldenseal, the information currently available suggests that concomitant intake of the herbal drugs addressed here is not a major risk for drugs that are metabolized by CYPs.

Abbreviations

$AUC_{(0-\infty)}$:	area under the concentration-time curve from 0 to infinity
C_{max}:	maximum serum concentration
CI:	confidence interval
CYP:	cytochrome P450 enzyme
EGCG:	epigallocatechin gallate
EMA:	European Medicines Agency
FDA:	Food and Drug Administration
GABA:	gamma-aminobutyric acid
GBE:	*Ginkgo biloba* extract
(d)GTE:	(decaffeinated) green tea extract
INR:	international normalized ratio of prothrombin time
LSS:	limited sampling strategy
p:	p value
Poly E:	Polyphenon E®
rac:	racemic
SJW:	St. John's wort
$t_{1/2}$:	elimination half-life

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Results

We identified 70 clinical studies in 69 publications. An overview of the data is presented in **Table 1** (at the end of the paper). Herb-drug interactions were present for 10 of the top 14 selling botanicals in the U.S. for 2006, including garlic with 2 drugs (chlorzoxazone, saquinavir), echinacea with 3 drugs (caffeine, midazolam, tolbutamide), ginkgo with 3 drugs (midazolam, omeprazole, tolbutamide), soy with 2 drugs (caffeine, theophylline), ginseng with 1 drug (debrisoquine), black cohosh with 1 drug (debrisoquine), St. John's wort with 19 drugs (alprazolam, atorvastatin, chlorzoxazone, cortisol, cyclosporine, desogestrel, ethinyl estradiol, gliclazide, imatinib, indinavir, ivabradine, mephenytoin, midazolam, norethindrone, omeprazole, quazepam, verapamil, voriconazole, and warfarin), kava with 1 drug (chlorzoxazone), and goldenseal with 2 drugs (debrisoquine, midazolam).

In addition to the 14 plants described in detail (see discussion), we found positive herb-drug interactions for *Angelica dahurica* with 1 drug (caffeine), *Scutelleria baicalensis* with 3 drugs (bupropion, chlorzoxazone, losartan), grapes/red wine with 4 drugs (buspirone, caffeine, dextromethorphan, losartan), and curcuma with 1 drug (caffeine).

The following detailed description of the respective botanicals is sorted in descending order of their U.S. sales ranking according to Blumenthal et al. [16].

Punti di incontro fra Medicina Allopatica e Medicina Naturale

- **Particolare attenzione allo Stile di vita**
- **Complementarietà nella prevenzione delle malattie cardio-vascolari**
- **Nelle discipline orientali e omeopatia, parallelismo possibile con effetto placebo-forza di volontà (es. nella riabilitazione medica si cerca il più possibile di motivare il paziente).**
- **Alcune terapie contro i tumori, non alternativi alla terapia tradizionale, ma come approcci complementari in grado di aiutare i pazienti a sentirsi meglio.**

Ricordati che il miglior medico é la natura : guarisce i due terzi delle malattie non parla male dei colleghi.

(Galeno)