

### **Transforming Oncology Care** Through Medically Integrated Collaboration 2025 NCODA INTERNATIONAL SPRING FORUM

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# About Herbs: The Role of Herbal Medicine in Cancer Care

### Yen Nien (Jason) Hou, PharmD, DiplOM, LAc

Herb Information Center Coordinator Manager, *About Herbs* Website Integrative Medicine Service Memorial Sloan Kettering Cancer Center



# OBJECTIVES

- 1. Discuss the practical application of herbal medicine in oncology
- 2. Review the development and implementation of the Herbal Oncology Program (HOP)
- 3. Summarize the role of traditional Chinese medicine (TCM) in Breast Cancer prevention and survival
- 4. Identify strategies to initiate patient conversations and address concerns about herbal medicine



# DISCLOSURES

There are no relevant conflicts of interest to disclose for the faculty and planners of this presentation:

- Yen Nien (Jason) Hou, PharmD, DiplOM, LAc
- Apiew Ojulu, PharmD, MS
- Tahsin Imam, PharmD
- Daisy Doan, PharmD



# Practical Application of Herbal Medicine in Oncology



### Supplements and Traditional Chinese Herbal Medicines (TCHM) **Prevalence of use among cancer patients**



70.4% (N = 2772) supplement use among cancer survivors 46.1% (N = 1355) supplement use **without** consulting health care providers 2020 Du, et al.



68% (N = 85) Asian immigrant cancer patients in NYC used TCHM concurrently with conventional treatment 13% (N = 85) communicated with healthcare providers 2020 Leng, et al.



### **How Patients Self-Inform**

 Internet, social media-based searches, along with family and friend recommendations

- General belief that natural products are safe
- But clinical information is quite limited
- And may not include potential herb-drug interactions (HDIs)
- Nor consider the unique and changing needs of cancer patients before, during, and after treatment



# QUESTION

Where do you usually search for information about herbs and supplements?

- a. Google
- b. ChatGPT
- c. About Herbs
- d. Natural Medicine
- e. PubMed



### About Herbs Website



### Free and evidence-based

For clinicians, patients, and caregivers

*With* evidence especially relevant to cancer patients *And* notes clinical relevance of potential HDIs





Internal survey conducted at Memorial Sloan Kettering Cancer Center

# Making Use of **About Herbs**

#### **Quick Start**

- Get familiar with popular herbs
- Get familiar with our latest traditional
   Chinese medicine
   (TCM) entries
- Use the Alphabet
   Directory and search
   bar to locate other
   herbs



Hou YN, Deng G, Mao JJ. Practical Application of "About Herbs" Website: Herbs and Dietary Supplement Use in Oncology Settings. Cancer J. 2019 Sep/Oct;25(5):357-366. doi: 10.1097/PPO.0000000000000403. PMID: 31567464; PMCID: PMC6777855.

### About Herbs Speaks to Target Audiences

To meet the specific needs of cancer patients and healthcare professionals



For Healthcare Profess	ionals	
Scientific Name		+
Clinical Summary		+
Purported Uses		+
Mechanism of Action		+
Warnings		+
Contraindications		+
Adverse Reactions		+
Herb-Drug Interactions		+
Herb Lab Interactions		+
Dosage (OneMSK Only)	Internal to MSK	+
References	Links to PubMed F	+ Refs
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### About Herbs Speaks to Target Audiences

#### Citations link to PubMed abstracts in the reference list

#### **Healthcare Professionals**

#### Herb-Drug Interactions

- Adenosine: The caffeine content may inhibit the hemodynamic effects of adenosine
- Anticoagulants / Antiplatelets: Theoretically, consumption of large amounts (.5-1 gald may provide enough vitamin K to antagonize the effects of anticoagulants and antiplate antiplate and antiplate antiplate antiplate antiplate
- agents, though this effect has not been reported in humans <sup>(29)</sup> <sup>(34)</sup>. Atropine: The tannin content may reduce the absorption of atropine
- Iron supplements: The tannin content in may reduce the bioavailability of iron. Green should be taken either 2 hours before or 4 hours following iron administration.
- Codeine: The tannin content may reduce the absorption of codeine <sup>(18)</sup>.
- Bortezomib: EGCG and other polyphenols can inhibit the therapeutic effect of bortez other boronic acid based proteasome inhibitors <sup>(37)</sup>.
- Tamoxifen: EGCG was shown to increase the oral bioavailability of tamoxifen, increasing the potential for their interactions <sup>(38)</sup>.
- Verapamil: The bioavailability of verapamil increased significantly in the pi thought to be due to P-glycoprotein inhibition by EGCG <sup>(39)</sup>.
- Irinotecan: A study found EGCG to inhibit transport of irinotecan and its n biliary elimination, resulting in their prolonged half-life which can increase
- Cytochrome P450 3A4 substrates: Green tea extract inhibits CYP 3A4 enz the intracellular concentration of drugs metabolized by this enzyme <sup>(43) (4</sup>
- UGT (Uridine 5'-diphospho-glucuronosyltransferase) substrates: Green tea enzymes in vitro and can increase the side effects of drugs metabolized b
- Acetaminophen: Green tea was shown to increase acetaminophen-induce

#### Green Tea



#### References

 Goldin EB, Lam P, Kardosh A, et al. Green tea polyphenols block the anticancer effects of bortezomib and other boronic acid based proteasome inhibitors. *Blood* 2009 Jun 4;113(23):5927-37.

38 Shin SC, Choi JS. Effects of epigallocatechin gallate on the oral bioavailability and pharmacokinetics of tamoxifen and its main metabolite, 4-hydroxytamoxifen, in rats. Anticancer Drugs. 2009 Aug;20(7):584-8.

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Blood. 2009 Jun 4;113(23):5927	'-37. doi: 10.1182/blc	od-2008-07-171389. Epub 2009	Feb 3.		Full text links
Green tea polyphe	nols block	the anticancer effe	cts of bortezomib and othe	er boronic acid-based	Plood Blood
proteasome innibi	tors.				Cause literature
Golden EB <sup>1</sup> , Lam PY, Kardos	h A, Gaffney KJ, C	adenas E. Louie SG, Petasis I	A, Chen TC, Schönthal AH.		Save items
Author information					Add to Favorites -
Abstract					

The anticancer potency of green tea and its individual components is being intensely investigated, and some cancer patients already selfmedicate with this "miracle herb" in hopes of augmenting the anticancer outcome of their chemotherapy. Bortezomit (BZM) is a proteasome inhibitor in clinical use for multiple myeloma. Here, we investigated whether the combination of these compounds would yield increased antitumor efficacy in multiple myeloma and glioblastoma cell lines in vitro and in vivo. Unexpectedly, we discovered that various green tea constituents, in particular (-)-epigallocatechin gallate (ESCG) and other polyphenols with 1,2-benzenediol moieties, effectively prevented tumor cell death induced by BZM in vitro and in vivo. This pronounced antagonistic function of EGCG was evident only with oronic acidbased proteasome inhibitors (BZM, MG-42C, PS-IX), but not with several non-boronic acid proteasome inhibitors (BZA), PSI-4, benRinavir). EGCG directly reacted with BZM and blocked its proteasome inhibitors (MG-42, PSI-4, but not with several non-boronic acid proteasome inhibitors (and PSI-2), PSI-4, but not with several non-boronic acid proteasome inhibitors (MG-42, PSI-4), but not with several non-boronic acid proteasome inhibitors (MG-42), PSI-4, benRinavir). EGCG directly reacted with BZM and blocked its proteasome inhibitory function; as a consequence, BZM could not trigger endoplasmic reticulum stress or caspase-7 activation, and did not induce tumor cell death. Taken together, our results indicate that green tea polyphenols may have the potential to negate the therapeutic efficacy of BZM and suggest that consumption of green tea products may be contraindicated during cancer therapy with BZM.

#### Comment in

Bortezomib and EGCG: no green tea for you? [Blood. 2009] From orbital hybridization to chemotherapeutics neutralization. [Blood. 2009] Therapeutic use of tea derivatives: all that glitters is not gold. [Blood. 2009]

#### Similar articles Therapeutic use of tea der is not gold.

Natural polyphenols antago activity of proteasome inhib Methylation suppresses the

inhibitory function of green Review Mechanisms of ca

green and t [Anticancer Age

Review [Proteasome inhibi apoptosis as new therapeut



### **Examples of Herb and Supplement Use**

#### But evidence is often limited or lacking

Appetite	Cognition	Fatigue	Immune function	Menopause symptoms	Nausea	Pain	Sleep	Stress/ Anxiety	Weight Ioss
Cannabis Ginger Shi Quan Da Bu Tang	Carnitine Ginkgo Ginseng Gotu Kola Rhodiola	Astragalus Carnitine CoQ10 Ginseng Mate Reishi Rhodiola	Astragalus Chaga Coriolus Ginseng Lentinan Maitake Reishi Shiitake Turmeric Vitamin C	Black Cohosh Chasteberry Dong Quai Flaxseed Maca Pollen Extract Red Clover Soy Wild Yam XYS	Astragalus Cannabis Ginger Peppermint	Arnica Bromelain Cannabis Capsaicin Devil's Claw Glucosamine Turmeric Vitamin B6 Willow Bark Yunnan Baiyao	Cannabis Chamomile Hops Kava Lavender Lemongrass L-Theanine Melatonin Passionflower Valerian	5-HTP Ashwagandha Cannabis Chamomile Kava Lavender Lemongrass Passionflower St John's Wort XYS	5-HTP Garcinia Green tea Mate Maitake Taurine
Rh	odiola Gir	ngko	Astragalus	Ginseng	Dong quai	Maca Fla	axseed	St John's wort	Maitake

Internal survey conducted at Memorial Sloan Kettering Cancer Center

### **Botanicals with Known HDIs and AEs**



HDIs	Liver toxicities	Immuno- modulating	Hormonal activity	Antioxidant	Photo- sensitizing	Bleeding risk	High in oxalates
Berberine	Black cohosh	Astragalus	Astragalus	Acai	St. John's wort	Dong quai	Cranberry
Cannabis	Chaparral	Chaga	Dong quai	Astragalus	Limes	Feverfew	Chaga
Isatis	Comfrey	Coriolus	Ginseng	Garlic		Garlic	Dandelion
Kava	Garcinia	Echinacea	Lavender	Grape seed		Ginger	Rhubarb
Oleandrin	Kava	Reishi	Red clover	extract		Ginkgo	Sheep sorrel
Red yeast rice	Noni		Soy	Graviola			Vitamin C
Reishi	Vitamin A			NAC			
St John's wort				Pomegranate			
				Vitamin C	St John's wort		
				Vitamin E			
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Red yeast rice	7	Astragalus	💛 💛 Soy	Graviola		Gingko	
		y		-		Cirigito	

Internal survey conducted at Memorial Sloan Kettering Cancer Center

### *About Herbs* New Monographs

Memorial Sloan Kettering Cancer Center. *Suan Zao Ren Tang.* About Herbs. <u>https://www.mskcc.org/cancer-care/integrative-medicine/herbs/suan-zao-ren-tang.</u> Accessed April 10, 2025.



Memorial Sloan Kettering Cancer Center. *Castor Oil*. About Herbs. <u>https://www.mskcc.org/cancer-care/integrative-medicine/herbs/castor-oil</u>. Accessed April 10, 2025.

Development and Implementation of the Herbal Oncology Program (HOP)



# QUESTION

Is there potential for integrating Eastern (traditional) and Western (conventional) medicine within an NCI-designated cancer center?

- a. Yes integration is feasible and could enhance patient care, but would require significant institutional support and evidence
- b. No challenges make integration unlikely in this setting
- c. Unsure / would need more data to evaluate





To advance the research and education of safe and appropriate use of herbs to improve the health and wellbeing of individuals impacted by cancer

Research : Clinical education : Evidence-informed practice

## **Interrelated Care Gaps Underscore Critical Needs**





Correa-Velez et al. *J Palliat Med* 2005; 8: 953–61; Evans et al. *BMC Complement Altern Med* 2007; 7: 25 Ge et al. *Int J Radiat Oncol Biol Phys* 2013; 85: e1–6; Gupta et al. *Support Care Cancer* 2005; 13: 912–9



To develop, implement and evaluate a novel program facilitating patientprovider communication about, and appropriate use of, herbal medicine at a large academic cancer center



# Herbal Formulary and Dispensary Process



P&T, MSK Pharmacy & Therapeutics

# **Shared Decision-Making with Patients**



- IM providers counseled patients
- Identified unmet symptom needs

## Prescribed TCM herbs when indicated



# **Data Evaluation and Patient Survey**

Medical record data of all participants: Feb 2019 – Jan 2022

- Symptoms
- Other concerns that motivated
- patients to seek herbal products
- Types and quantities of dispensed TCM products
- Demographics

Brief survey\* approved by MSK IRB to herbal Rx recipients: May – Aug 2021

- Symptoms or concerns patients hoped to address
- Satisfaction with HOP program and products dispensed
- Whether patients experienced AEs
- How likely would patients recommend the dispensary program

Answer options were multiple choice, Yes/No, or 5-point Likert scales: extremely satisfied/likely to extremely dissatisfied/unlikely. Distributed via Research Electronic Data Capture (REDCap<sup>™</sup>) web application



Harris et al. J Biomed Inform 2009; 42: 377-81; Vanderbilt University REDCap (Research Electronic Data Capture) 2018

# Patient Data

851 Outpatients with diverse cancers

712 (84%) in active treatment

Median Age61 y (18–98)Female606 (71%)White594 (70%)Insured498 (59%)





# **TCM Prescriptions/Common Symptoms**



### Survey Results: May – Aug 2021

### Symptoms Participants Hoped to Address (n= 103)







## Limitations



Project based on methods for program development, implementation, and evaluation in a real-world setting, not a formal research protocol



Survey findings based on a patient sample self-selected for outcome evaluation may not represent the entire study population

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Only immediate symptom relief with herbal products was evaluated; durability not known





- Demonstrates feasibility of integrating herbal medicine into an academic oncology setting
- High patient satisfaction
- Limited adverse events
- Elucidates future research directions



### **Publications on Dispensary Products**

Liou KT, et al. Pain Med. 2021 Jun 4;22(6):1435-1440.

#### Yang M, et al. Phytomedicine. 2021 Feb;82:153459.





### **About Herbs Monographs on Dispensary Products**

### Ma Zi Ren Wan

Purported Benefits, Side Effects & More



#### **Common Names**

- Hemp Seed Pill
- Hemp Seed Formula
- Mashiningan
- TJ-126

### Xiao Yao San

Purported Benefits, Side Effects & More



#### **Common Names**

- Free and Easy Wanderer
- Rambling Powder
- Jia Wei Xiao Yao San
- Dan Zhi Xiao Yao San
- Augmented rambling powder
- Kamishoyosan
- TJ-24

### **Shen Ling Bai Zhu San**

Purported Benefits, Side Effects & More



### Suan Zao Ren Tang

Purported Benefits, Side Effects & More



#### **Common Names**

- Ginseng & Atractylodes Formula
- Samryungbaekchul-san
- Jinrvobvakuiutsu-san

#### **Common Names**

- Suanzaoren
- Semen Ziziphus Spinosae
- Ziziphus
- Sour Jujube Decoction
- Ziziphus Decoction Formula
- Tabellae Suanzaoren Tang

Internal survey conducted at Memorial Sloan Kettering Cancer Center

# Role of Traditional Chinese Medicine (TCM) in Breast Cancer Prevention and Survival



## Taiwan National Health Insurance Research Database (NHIRD)

To assess the evidence surrounding TCM herbal use in breast cancer care, with a focus on both prevention and mortality





# Prevention

N = 17,583; 55-79 y.o. menopausal women on exogenous hormone – coadministration of hormone regimen with TCM herbs did not elevate breast cancer risk

Presence of breast cancer during the follow-up period	HT users who did not use a Chinese medicine. Number of cases/population	HT users coprescribed a Chinese medicine, Number of cases/population	HT users coprescribed a Chinese medicine/HT users who did not use a Chinese medicine HR (95% CI)	Presence of breast cancer during the follow-up period	HT users who did not use a Chinese medicine. Number of cases/population	HT users coprescribed a Chinese medicine, Number of cases/population	HT users coprescribed a Chinese medicine/HT users who did not use a Chinese medicine aHR (95% CI)
HT* use at baseline				HT* use at baseline		10.00	
Estrogen-alone				Estrogen-alone			
Current users	3/53	2/117	0.30 (0.05–1.81)	Current users	3/53	2/117	1.00
Last use 1-3 years previously	0/211	3/249	-	Last use 1-3 years previously	0/211	3/249	0.22 (0.05-0.93)
Last use 4-5 years previously	1/192	1/157	1.21 (0.08–19.41)	Last use 4-5 years previously	1/192	1/159	0.19 (0.04-1.00)
Last use >=6 years previously	2/710	1/395	0.90 (0.08–9.91)	Last use >=6 years previously	2/710	1/395	0.09 (0.02-0.39)
Mixed type <sup>†</sup>				Mixed type <sup>†</sup>			
Current users	5/69	7/246	0.39 (0.13–1.24)	Current users	5/69	7/246	1.00
Last use 1-3 years previously	1/69	8/192	2.87 (0.36-22.98)	Last use 1-3 years previously	1/69	8/192	0.91 (0.38-2.15)
Last use 4-5 years previously	0/118	0/614	1770	Last use 4-5 years previously	0/118	0/614	
Last use >=6 years previously	16/836	11/1,081	0.53 (0.25–1.15)	Last use >=6 years previously	16/836	11/1,081	0.37 (0.19–0.73)

\*HT refers to hormonal therapy.

<sup>†</sup>Mixed type refers to the estrogen-alone (E-alone); estrogen together with progesterone (E + P); other preparations, which included progesterone only and vaginal and other local treatments and combinations of the above preparation types.

\*HT refers to hormonal therapy.

<sup>†</sup>Mixed type refers to the estrogen-alone (E-alone); estrogen together with progesterone (E + P); other preparations, which included progesterone only and vaginal and other local treatments and combinations of the above preparation types. aHR refers to the hazard ratios adjusted by age and number of chronic diseases.

Tsai YT, et al. Evid Based Complement Alternat Med. 2014; 2014;2014:683570.



N = 184,386; female with other medical conditions – adjusted hazard ratios for breast cancer were **0.57** (95% confidence interval [CI] 0.50–0.65) and **0.36** (95% CI 0.28–0.46) in women using CHPs and SWT, respectively.

	Non-TCM users				T	CM users			
	No. of subjects	No. of events	ID <sup>*</sup> (per 10,000 patient–years) (95% CI)	No. of subjects	No. of events	ID <sup>*</sup> (per 10,000 patient–years) (95% CI)	Crude HR (95% CI) in association with TCM users	Adjusted HR <sup>+</sup> (95% CI) in association with TCM users	
Total	40,092	635	1.73 (1.60–1.86)	40,092	349	0.85 (0.76–0.94)	0.55 (0.48–0.63)	0.57 (0.50-0.65)	
		-TCM users		SI	WT users				
	No. of subjects	No. of events	ID <sup>*</sup> (per 10,000 patient-years) (95% CI)	No. of subjects	No. of events	ID <sup>*</sup> (per 10,000 patient- years) (95% CI)	Crude HR (95% CI) in association with SWT users	Adjusted $\text{HR}^{\dagger}$ (95% CI) in association with SWT users	
Total	40,092	635	1.73 (1.60–1.86)	13,578	73	0.63 (0.57–0.69)	0.34 (0.27–0.43)	0.36 (0.28-0.46)	

AHR = adjusted hazard ratio, CI = confidence interval, ICD-9 = International Classification of Diseases, Ninth Revision, ID = incidence density, IR = incidence rate, HR = hazard ratio, TCM = traditional Chinese medicine, SWT = *siwutang*.

Based on Poisson assumption.

\* Based on Cox proportional hazard regression with adjustment for age, geographic area, urbanization status, history of diabetes, obesity, oophorectomy, endometriosis, myoma, irregular menstrual, premenstrual syndrome, and polycystic ovary syndrome, abortion, and HT usage.



N = 33,828 matched 1:10 female with diabetes mellitus II – Hazard ratio of **0.57** (95%CI: 0.45–0.73) in patients using TCM excluding Di Huang Wan series; and hazard ratio of **0.45** (95%CI: 0.34–0.59) in patients using TCM including Di Huang Wan series

	Age	ed 20–79	Age	d 20–54	Α	ged 55–79
	Case/control	HR (95%CI)	Case/control	HR (95%CI)	Case/control	HR (95%CI)
Antidiabetics						
None	124/509	1	88/330	1	36/179	1
Metformin users						
Metformin alone	20/363	0.79 (0.47-1.32)	14/242	0.93 (0.49–1.74)	6/121	0.40 (0.15-1.09)
Metformin+1	81/903	0.82 (0.58-1.16)	39/549	0.79 (0.49-1.26)	42/354	0.89 (0.52-1.51)
Metformin+2 above	171/2206	0.50 (0.36-0.67)	80/1,148	0.48 (0.32-0.72)	91/1058	0.52 (0.32-0.85)
Metformin nonusers						
1 drug	26/206	1.42 (0.89–2.28)	12/104	1.62 (0.83-3.14)	14/102	1.41 (0.71–2.79)
2 drugs	5/59	0.88 (0.35-2.20)	2/32	0.76 (0.18-3.18)	3/27	1.03 (0.31–3.50)
3 above	1/34	0.23 (0.03-1.65)	0/11	_	1/23	0.33 (0.05-2.50)
TCM						
TCM < 500 a	317/2766	1	173/1.510	1	144/1256	1
TCM exclude DHWS*	44/587	0.57 (0.45-0.73)	29/366	0.54 (0.39-0.76)	15/221	0.57 (0.40-0.82)
DHWS user	67/927	0.45 (0.34-0.59)	33/540	0.35 (0.23-0.51)	34/387	0.54 (0.37-0.79)
Hormone usage						
No	375/4132	1	204/2,294	1	171/1838	1
Estrogen only	34/90	4.04 (2.65-6.14)	18/67	2.29 (1.24-4.24)	16/23	8.49 (4.77-15.11)
Progesterone only	7/38	1.52 (0.56-4.10)	6/36	0.98 (0.31-3.11)	1/2	12.65 (1.71-93.78)
Estrogen plus progesterone	12/20	5.04 (2.37-10.71)	7/19	2.20 (0.70-6.90)	5/1	42.77 (13.42–136.31

\* DHWS refers to *Di Huang Wan* series.

#### **Wu CT**, et al. *Medicine (Baltimore).* **2018**;97(31):e11600.



N = 137,048 matched 1:3 female with other medical conditions – exposure to *Angelica sinensis* (AS; aka Dang Gui) had a *weak but significant protective effect* on breast cancer risk, which can ease patient concerns over potential carcinogenic effect of AS

	Cases N = 34262	Controls $N = 102786$	Adjusted OR (95% CI)	Р
	No. (%)	No. (%)		
Angelica sinensis	exposure			
No	16879 (49.3)	50767 (49.4)	1.00 (REF)	
Yes	17383 (50.7)	52019 (50.6)	0.95 (0.93-0.98)	< 0.0001
Exposure dose (	grams)			
0.1-9.9	8017 (23.4)	24271 (23.6)	0.97 (0.93-1.00)	< 0.06
10-29.9	4917 (14.4)	14827 (14.4)	0.93 (0.89-0.97)	<0.001
≧30	4039 (11.8)	11612 (11.3)	0.96 (0.91-1.00)	< 0.06
			Trend test: $\beta = -0.024$	<0.001

Crude and adjusted ORs of breast cancer in association with Angelica sinensis exposure.

Abbreviations: CI, confidence interval; OR, odds ratio.

Adjusted OR: adjusted for residential area, monthly salary, gynecology cancer, benign breast/uterine tumor, metabolic disease and estrogen/progesterone exposure.

Note: the total exposure dose contain Angelica sinensis compound dose x0.1 and Angelica sinensis single herb dose x1.



#### **<u>Chen JY</u>**, et al. *JTradit Complement Med.* **2019**;10(5):454-459.

N = 137,048 matched 1:3 female with other medical conditions – exposure to *Angelica sinensis* (AS; aka Dang Gui) had a *weak but significant protective effect* on breast cancer risk, which can ease patient concerns over potential carcinogenic effect of AS

Stronger protective effects were noted among women who began using Angelica sinensis at ages 47–55 (aOR: 0.93, 95% CI: 0.88–0.98).

_	-		-	<u> </u>	
Age at initial use of Agelica sinensis		Cases N = 34262	Controls $N = 102786$	Adjusted OR (95% CI)	Р
		No. (%)	No. (%)		
	Non-exposure	16879 (49.3)	50767 (49.4)	1.00 (REF)	
	Exposure before menopause (age ≤47v)	9119 (26.6)	27152 (26.4)	0.96(0.92 - 1.00)	0.04
	Exposure during menopause (47y < age<55y)	4152 (12.1)	12614 (12.3)	0.93 (0.88-0.98)	<.001
	Exposure after menopause (age≧55y)	4112 (12.0)	12253 (11.9)	0.97 (0.92-1.02)	0.25
	Non-exposure Exposure before menopause (age $\leq 47y$ ) Exposure during menopause (47y < age<55y) Exposure after menopause (age $\geq 55y$ )	No. (%) 16879 (49.3) 9119 (26.6) 4152 (12.1) 4112 (12.0)	$\frac{N = 102786}{No. (\%)}$ 50767 (49.4) 27152 (26.4) 12614 (12.3) 12253 (11.9)	1.00 (REF) 0.96 (0.92–1.00) 0.93 (0.88–0.98) 0.97 (0.92–1.02)	0.04 <.00

Crude and adjusted ORs of breast cancer in association with initial use of Angelica sinensis at various ages.

Abbreviations: CI, confidence interval; OR, odds ratio; y, years old.

Adjusted OR: adjusted for age, residential area, monthly salary, gynecology cancer, benign breast/uterine tumor, metabolic disease and estrogen/progesterone exposure.



**<u>Chen JY</u>**, et al. *JTradit Complement Med.* **2019**;10(5):454-459.

# Mortality

N = 729 locally advanced or metastatic BC patients – adjunctive TCM therapy may lower the risk of death in patients with advanced breast cancer. HR = 0.5 (0.35-0.73), compared to non-users



**TABLE 2.** Unadjusted and Adjusted Cox Proportional Hazards Model Analysis of the Mortality of Patients With Breast Cancer

		Univariate Analysis	S	Multivariate Analysis			
Variable	HR	95% CI	Р	aHR <sup>a</sup>	95% CI	Р	
TCM use							
Nonusers (<30 d)	1			1			
TCM users (≥30 d)	0.53	0.37-0.77	<.001	0.50	0.35-0.73	<.001	
30-180 d	0.58	0.36-0.95	.03	0.55	0.33-0.90	.02	
>180 d	0.48	0.29-0.81	.006	0.46	0.27-0.78	.004	
Age (per 1 y)	1.01	1.00-1.02	.12	1.00	0.99-1.02	.58	
Congestive heart failure	1.91	0.98-3.72	.06	1.31	0.67-2.56	.44	
Distant metastases	3.10	2.44-3.94	<.001	2.44	1.84-3.24	<.001	
Surgery							
None	1			1			
Breast-conserving surgery	0.42	0.30-0.61	<.001	0.56	0.38-0.81	.002	
Mastectomy	0.33	0.25-0.43	<.001	0.54	0.40-0.73	<.001	
Hormonal or targeted biologic therapy	1.46	1.10-1.92	.01	1.06	0.80-1.41	.69	
Radiotherapy	1.36	1.06-1.75	.02	1.56	1.21-2.01	<.001	

Abbreviations: 95% CI, 95% confidence interval; aHR, adjusted hazards ratio; HR, hazards ratio; TCM, traditional Chinese medicine. <sup>a</sup>Adjusting for all variables listed.





# Mortality (cont'd)

N = 872 ER+ BC patients on adjuvant hormonal therapy per NHI reimbursement – a potential advantage of TCM on BC-associated mortality, and TCM use did not compromise medical adherence to HT.  $\geq$ 3/yr TCM visit & 1 90-day supply of CHP/yr: HR = **0.26** 





Chan PW, et al. Phytomedicine. 2021;80:153365.

# Mortality (cont'd)

N = 10,774 newly diagnosed breast cancer (BC) patients – San-Huang-Xie-Xin-Tang (SHXXT) and its constituents showed promising therapeutic effects against BC

	No	Non-CHM User			CHM User			
Characteristics	Event	Event Person IR <sup>+</sup> Event Person IR <sup>+</sup> Years IR <sup>+</sup>		Crude HR	Adjusted HR ‡			
Total	1141	27,576	41.38	456	33,488	13.62	0.33 (0.3–0.37) ***	0.41 (0.37–0.46) ***
Age group								
18–39	171	4879	34.92	75	6083	12.33	0.35 (0.27–0.46) ***	0.4 (0.3–0.54) ***
40–59	741	18,929	39.15	288	22,641	12.72	0.33 (0.29–0.38) ***	0.41 (0.35–0.47) ***
$\geq 60$	229	3750	61.07	93	4765	19.52	0.33 (0.26–0.42) ***	0.35 (0.27–0.45) ***
: represented adjusted hazard ratio:	C	CHM Prescription –			Iortality		HR (959	% CI)
nutually adjusted for CHM use, age group, urbanization level, CCI score,	CI				No. of Event		Crude	Adjusted <sup>+</sup>
reatment, and drugs by Cox	Nor	Non-CHM user			1141		1 (reference)	1 (reference)
noportional nazard regression.	Sing	gle constitu	ient					
	R	Rhizoma Rhei			278		0.36 (0.31–0.41) ***	0.42 (0.37–0.48) ***
	R	adix Scutel	laria	3958	327		0.32 (0.28–0.36) ***	0.40 (0.36–0.46) ***
	R	Rhizoma Coptidis		2644	215		0.31 (0.27–0.36) ***	0.39 (0.34–0.45) ***
	Con	npounds						
		SHXXT			33		0.25 (0.18–0.36) ***	0.32 (0.22–0.45) ***
	R R Con	adix Scutel hizoma Co npounds SHXXT	laria ptidis	3958 2644 489	327 215 33		0.32 (0.28–0.36) *** 0.31 (0.27–0.36) *** 0.25 (0.18–0.36) ***	0.40 (0.36–0.46) ** 0.39 (0.34–0.45) ** 0.32 (0.22–0.45) **

Abbreviations: CHM, Chinese herbal medicine; HR, hazard ratio; CI, confidence interval. Crude HR represented relative hazard ratio. + Adjusted HR represented adjusted hazard ratio: mutually adjusted for age group, urbanization level, CCI score, treatment, and drugs by Cox proportional hazard regression. \*\*\* p < 0.001.

CHM – Chinese herbal medicine



Winardi D, et al. Cancers (Basel). 2023;15(4):1213.

# Mortality (cont'd)

N = 10,774 newly diagnosed breast cancer (BC) patients – San-Huang-Xie-Xin-Tang (SHXXT) and its constituents showed promising therapeutic effects against BC



cancer patients.

Characteristics	N	Mortality	HR (95% CI)	
		No. of Event	Crude	Adjusted $^{\dagger}$
Non-CHM users	5387	1141	1 (reference)	1 (reference)
CHM users				
30-90 days	3209	288	0.36 (0.31-0.40) ***	0.44 (0.38–0.50) ***
90-180 days	1233	106	0.33 (0.27-0.41) ***	0.41 (0.33-0.50) ***
>180 days	945	62	0.26 (0.20-0.33) ***	0.31 (0.24–0.40) ***
p for trend			<0.0001	<0.0001

The risk of mortality rate stratified by the cumulative days of CHM use among breast

Abbreviations: CHM, Chinese herbal medicine; HR, hazard ratio; CI, confidence interval. Crude HR represented relative hazard ratio. † Adjusted HR represented adjusted hazard ratio: mutually adjusted for age group, urbanization level, CCI score, treatment, and drugs by Cox proportional hazard regression. \*\*\* p < 0.001. The risk of mortality rate stratified by the annual average CHM dose among breast cancer patients.

Annual Average CHM Dose (g)	N	Mortality	HR (95% CI)	
		No. of Event	Crude	Adjusted <sup>†</sup>
Non-CHM users	5387	1141	1 (reference)	1 (reference)
CHM users				
<35.1 (g)/year	1346	140	0.42 (0.35-0.50) ***	0.50 (0.42–0.60) ***
35.1-67.2 (g)/year	1346	123	0.36 (0.30-0.44) ***	0.43 (0.35–0.51) ***
67.2-147 (g)/year	1340	113	0.33 (0.27-0.40) ***	0.39 (0.32–0.48) ***
>147 (g)/year	1355	80	0.23 (0.18–0.29) ***	0.30 (0.24–0.38) ***
p for trend			<0.0001	<0.0001

Abbreviations: CHM, Chinese herbal medicine; HR, hazard ratio; CI, confidence interval. Crude HR represented relative hazard ratio.  $\dagger$  Adjusted HR represented adjusted hazard ratio: mutually adjusted for age group, urbanization level, CCI score, treatment, and drugs by Cox proportional hazard regression. \*\*\* p < 0.001.

CHM – Chinese herbal medicine



Winardi D, et al. Cancers (Basel). 2023;15(4):1213.

# Identify Strategies to Initiate Patient Conversation & Address Concerns About Herbal Medicines



## General Guidelines Think SĀF-TI First



**Standardization** Most herbal products are not standardized, so impossible to compare potency

**A**bsorption

Herbal constituents that are not absorbed have no benefits

**F**unction

**T**oxicity

What are perceived benefits and how well have they been studied?

Some products may be contaminated with heavy metals, microbes, or unknown substances

Interactions

Herb-drug interactions may be underreported and/or not adequately studied



Internal survey conducted at Memorial Sloan Kettering Cancer Center

#### Major categories of

#### Herb–Drug Interactions

Unintended or unwanted effects include:

Loss of drug efficacyIncreased toxicities

S	Antioxidants vs Chemotherapeutic Agents	Herbs to avoid before surgery for bleeding
Phytoestr Hormona • May st growth • Soy vs	<ul> <li>Can interfere with chemotherapy efficacy</li> <li>Grape seed vs cisplatin</li> <li>Standard Standard</li> <li>Increases bleeding risk</li> <li>Increases bleeding risk</li> <li>Garlic vs Warfarin</li> <li>Immunostimulant Herbs vs Immunosuppressants</li> </ul>	or anesthesia risks • Feverfew • Garlic • Ginger • Ginkgo • Kava • Saw palmetto • St. John's wort
	<ul> <li>Increased rejection risk after bone marrow or organ transplant</li> <li>Astragalus vs cyclophosphamide</li> </ul>	• Valerian



# Turkey Tail Mushroom (Coriolus versicolor)

Mushroom (fruiting body) VS





Benson KF, et al. BMC Complement Altern Med. 2019;19(1):342.



Real Mushrooms. https://www.realmushrooms.com/medicinal-mushroom-benefits-fruiting-body-vs-mycelium/. Accessed March 2025.

# Turkey Tail Mushroom (Coriolus versicolor)



**IMMUNE CELLS** TLRs: 2, 4, 5, 6, 7 TLRs: 2, 4 **NFKB** pPI3K AP-1 NFKB dendritic cells macrophages **PBMCs** cytokine production cytokine production maturation and activation ex. IL-1β, IL-6, TNF-α ex. IL-2, IL-12, IL-8, MIP-1 anti-viral cytokine phagocytosis proliferation rate production ↑ production of antibodies 1 iNOS, NO, ROS by B cells Immunostimulatory effects Jedrzejewski T, et. al. Int J Mol Sci. 2023;24(5):4864.

Coriolus versicolor

Anti-cancer potential of *C. versivolor* polysaccharides Habtemariam S, et al. *Biomedicines*. 2020;8(5):135.

### Turkey Tail Mushroom (Coriolus versicolor)

< Share V

### **Coriolus versicolor**

**Purported Benefits, Side Effects & More** 



For Patients & Caregivers

#### **Common Names**

- PSK
- PSPVPS
- Turkey Tail
- Yun Zhi
- Kawaratake
- Krestin

Jump to:

For Healthcare Professionals

#### **Adverse Reactions**

Rare: Dark colored stools not originating from occult blood <sup>(21)</sup>, darkening of fingernails <sup>(22)</sup>, and low-grade hematological and gastrointestinal toxicities when used in conjunction with chemotherapy <sup>(3)</sup>. However, such effects may be caused by the chemotherapy agents themselves.



Memorial Sloan Kettering Cancer Center. *Coriolus versicolor*. About Herbs. <u>https://www.mskcc.org/cancer-care/integrative-medicine/herbs/coriolus-versicolor</u>. Accessed April 10, 2025.

# Ma Zi Ren Wan (MZRW; aka Hemp Seed Pill)



Huo Ma Ren Hemp seed Cannabis Fructus **33%** 





Xing Ren Apricot seed Armeniacae Semen Amarum



Feng Mi Honey Apis Mel



Zhi Shi Unripe Bitter Orange Aurantii Fructus Immaturus

Da Huang Chinese Rhubarb root Rhei Radix et Rhizoma



Hou Pu Magnolia bark Magnoliae Officinalis Cortex



Bai Shao White Peony root Paeoniae Radix Alba





Internal survey conducted at Memorial Sloan Kettering Cancer Center

### Ma Zi Ren Wan (Hemp Seed Pill) Calculation for HDI Safety with MZRW

#### CASE STUDY

**Taxol**: Strong substrate of CYP3A4, CYP2C8

CBD MW 314.464 g/mol

Bottom line:

Will not interfere with
 Taxol via CYP3A4

 Will not interfere with CYP2C8



*Taxus brevifolia* (Pacific yew)



Paclitaxel (Taxol), a widely used cancer drug originally isolated from the bark of the Pacific yew tree

#### In vitro, <u>Yamaori S, et al. 2011</u><sup>1</sup>:

- IC50 of CBD on CYP3A4 (competitive inhibition Ki=1) is 11.7uM
- 11.7umol/L x 314.464 ug/umol = 3679 ug/L → 3679 ng/mL

#### In humans:

 Millar SA, et al. 2018<sup>2</sup>: A study of *oral CBD* dose involving 8 male and female cannabis smokers; Reported a mean Cmax of 77.9 ng/mL and mean Tmax of 3.0 h

 Taylor L, et al. 2018<sup>3</sup>: Showed Cmax was 541.2 ng/mL and AUC τ was 3236 ng·h/mL



1. Yamaori S, et al. Life Sci. 2011;88(15-16):730-736. 2. Millar SA, et al. Front Pharmacol. 2018;9:1365. 3. Taylor L, et al. CNS Drugs. 2018;32(11):1053-1067.

### Ma Zi Ren Wan (MZRW)

#### Ma Zi Ren Wan

Purported Benefits, Side Effects & More



#### **Common Names**

< Share v

- Hemp Seed Pill
- Hemp Seed Formula
- Mashiningan
- TJ-126

### **Adverse Reactions**

Abdominal pain, cramping, bloating, diarrhea, gas, nausea, vomiting, headache and dizziness (5) (6) (14) (15) (8).

Jump to: For Patients & Caregivers

For Healthcare Professionals

SPRING FORUM

Memorial Sloan Kettering Cancer Center. *Ma Zi Ren Wan*. About Herbs. <u>https://www.mskcc.org/cancer-care/integrative-medicine/herbs/mazirenwan</u>. Accessed April 10, 2025.

# QUESTION & ANSWERS

# About Herbs: The Role of Herbal Medicine in Cancer Care

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## CE CODES

# About Herbs: The Role of Herbal Medicine in Cancer Care

