

**COMPLEMENTARY MEDICINE USE DURING CANCER TREATMENT AND
POTENTIAL HERB-DRUG INTERACTIONS FROM A CROSS-SECTIONAL
STUDY IN AN ACADEMIC CENTRE.**

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SUPPLEMENTARY INFORMATION

SUPPLEMENTARY QUESTIONNAIRE S1

QUESTIONNAIRE

ETUDE SUR L'UTILISATION DES MÉDECINE COMPLÉMENTAIRE EN ONCOLOGIE

N° d'identifiant pour l'étude (ex. 008):

Date de l'entretien (jj/mm/aa) :

Dans ce questionnaire, le terme de *médecine complémentaire* est défini comme suit : il s'agit des médecines qui ne sont pas dans la tradition du pays ou qui ne sont pas intégrés dans le système de santé dominant. Cela regroupe donc aussi d'autres termes utilisés comme médecine alternative, douce, parallèle, naturelle ou holistique. Si vous ne savez pas ce qu'est une médecine complémentaire, vous trouverez quelques exemples à la question 12. Dans ce questionnaire, nous nous intéressons à toute forme de prescription de médecine complémentaire, que ce soit par un médecin, un pharmacien, un thérapeute ou un traitement que vous avez pris vous-même sans recommandation d'un professionnel de santé.

Questions

1. Age :

2. Sexe : homme femme

3. Ethnie :

- | | |
|-----------------------------|--------------------------|
| Europe | <input type="checkbox"/> |
| Afrique | <input type="checkbox"/> |
| Amérique centrale et du sud | <input type="checkbox"/> |
| Amérique du nord | <input type="checkbox"/> |
| Asie | <input type="checkbox"/> |
| Océanie | <input type="checkbox"/> |
| Inconnu / apatride | <input type="checkbox"/> |
| Ne souhaite pas répondre | <input type="checkbox"/> |

4. Dernière formation suivie :

- | | |
|-------------------|--------------------------|
| Ecole obligatoire | <input type="checkbox"/> |
| Gymnase | <input type="checkbox"/> |
| Apprentissage | <input type="checkbox"/> |
| Haute école | <input type="checkbox"/> |
| Université | <input type="checkbox"/> |

5. Etes-vous au bénéfice d'une assurance complémentaire qui couvre des thérapies de médecine complémentaire :

Oui



Non
Ne sais pas

6. Etat civil :

Célibataire
Marié ou partenariat enregistré
Séparé/divorcé
Ne souhaite pas répondre

7. **Au cours de votre vie**, avez-vous déjà eu recours à une/des médecine(s) complémentaire(s)?

Oui
Non

Si oui, passez à la question 9. Si non, passez à la question 8.

8. Vous n'avez jamais eu recours à des médecines complémentaires parce que (plusieurs réponses possibles) :

Vous n'y croyez pas
C'est trop cher
Vous avez entendu des avis négatifs
Cela ne vous intéresse pas
Vous ne connaissez pas assez bien ce sujet

Autre (spécifier) :

.....
.....

Si vous n'avez jamais eu recours à de la médecine complémentaire, nous vous demandons de répondre encore aux questions 21 et 22.

9. **Depuis que votre cancer a été diagnostiqué**, avez-vous eu recours à une/des médecine(s) complémentaire(s) ?

Oui
Non

10. **Actuellement**, avez-vous recours à une/des médecine(s) complémentaire(s) ?

Oui
Non



11. Si oui, laquelle (plusieurs réponses possibles) :

- Acupuncture
- Médecine traditionnelle chinoise avec herbes chinoises
- Médecine ayurvédique
- Compléments alimentaires
(oligo-éléments, vitamines et/ou minéraux)
- Homéopathie
- Réflexologie
- Aromathérapie/huiles essentielles
- Hypnose
- Méditation
- Naturopathie
- Phytothérapie
- Reiki
- Yoga
- Thé vert
- Huile de poisson

Autre (spécifier laquelle) :

.....
.....
.....

12. Si vous prenez un(des) médicament(s) de la médecine complémentaire *ingérées* ou *injectées*, pouvez-vous mentionner le(s) noms commercial(ux) ou le nom de la/les substance(s), les doses, les dates de prises et les raisons de leur utilisation?

Substance/ Nom commercial	Dose	Période(s)/ Dates de prises	Indication* (1-5)

*Indication : pour quelle raison prenez-vous ce traitement de médecine complémentaire (plusieurs réponses possibles)?

1. Prévention de la rechute
2. Améliorer l'immunité
3. Traiter le cancer
4. Diminuer les effets secondaires de la chimiothérapie
5. Autre (spécifier) :



13. Pour vous, comment agissent les traitements de médecine complémentaire que vous prenez ? *(noter les mots employés par le patient)*

.....
.....
.....
.....

14. Qui vous a recommandé de suivre un traitement de médecines complémentaires pendant le traitement contre le cancer ?

- Famille/amis
- Médecin de famille
- Médecin oncologue
- Pharmacien
- Thérapeute complémentaire
- Médias (journal, radio, télévision, internet,...)
- Choix personnel

Autre (spécifier) :

.....
.....

15. Que pensez-vous des affirmations suivantes : Les traitements de médecine complémentaire que je prends sont très efficaces :

tout à fait d'accord d'accord ni d'accord, ni pas d'accord pas d'accord pas du tout d'accord

16. Les traitements de médecine complémentaire que je prends peuvent avoir des effets secondaires :

tout à fait d'accord d'accord ni d'accord, ni pas d'accord pas d'accord pas du tout d'accord

Si oui, lesquels redoutez-vous le plus ?

.....
.....

17. Les traitements de médecine complémentaire que je prends peuvent avoir un effet **négatif** sur le traitement du cancer :

tout à fait d'accord d'accord ni d'accord, ni pas d'accord pas d'accord pas du tout d'accord

Si oui, que craignez-vous le plus ?

.....
.....



18. Les traitements de médecine complémentaire que je prends peuvent avoir un effet **positif** sur le traitement du cancer :

tout à fait d'accord d'accord ni d'accord, ni pas d'accord pas d'accord pas du tout d'accord

Si oui, quel effet positif principal en attendez-vous ?

.....
.....

19. Je dispose de suffisamment d'informations sur les **bénéfices** des médecines complémentaires que je prends :

tout à fait d'accord d'accord ni d'accord, ni pas d'accord pas d'accord pas du tout d'accord

20. Je dispose de suffisamment d'informations sur les **risques** des médecines complémentaires que je prends :

tout à fait d'accord d'accord ni d'accord, ni pas d'accord pas d'accord pas du tout d'accord

21. Est-ce qu'il vous a été demandé si vous utilisez une médecine complémentaire

Par votre médecin oncologue ?

Par un infirmier/infirmière en oncologie ?

Oui
Non

Oui
Non

22. Est-ce qu'il vous a été proposé d'utiliser une médecine complémentaire

Par votre médecin oncologue ?

Par un infirmier/infirmière en oncologie ?

Oui
Non

Oui
Non

Si oui, laquelle/ lesquelles :

.....
.....

23. Avez-vous dit que vous utilisez une médecine complémentaire

A votre médecin oncologue ?

A un infirmier/infirmière en oncologie ?

Oui
Non

Oui
Non



24. Si oui la question 23, votre médecin oncologue/ infirmier/ère connaissait-il/elle cette thérapie ?

- Oui
Non
Ne sais pas

25. Si oui à la question 23, comment a-t-il/elle répondu :

- Encouragé à continuer le traitement de médecine complémentaire
Demandé d'arrêter le traitement de médecine complémentaire
N'a pas fait de recommandation

Autre (spécifier) :

.....
.....

26. Si non à la question 23, pourquoi n'en avez-vous pas parlé :

- Parce qu'il/elle ne me l'a pas demandé
Il/elle ne comprendrait pas
Il/elle ne serait pas content
J'ai oublié de le mentionner
Cela n'a pas d'importance de le dire

Autre (spécifier) :

.....
.....

27. Si votre médecin oncologue jugeait inapproprié de continuer la prise concomitante de médecines complémentaires en même temps que le traitement anticancéreux, continueriez-vous à les utiliser ?

- Oui, dans tous les cas
Non, j'arrêtera sans problème
J'aurais besoin de justifications avant de décider
Je n'arrêtera que si les risques de continuer sont graves

Souhaitez-vous préciser votre réponse :

.....
.....
.....
.....



ANNEXE 2 : DONNÉES MÉDICALES DU PATIENT

N° d'identifiant pour l'étude (ex. 008):

Age :

Sexe : homme femme

Poids (kg) :

*Insuffisance rénale actuelle ? oui non ?

*Insuffisance ou perturbation actuelle des tests hépatiques? oui non ?

- * Oui : si figure dans la liste des diagnostics récents (<1an) selon le dossier médical
- Non : si fonction organique précisée comme normale dans le dossier médical (< 1an)
- ? : si aucune précision n'est donnée dans le dossier médical ou que la dernière évaluation des fonctions organiques date de >1 an

Type de cancer:

- Nez
- Gorge ou oreille
- Cerveau
- Sein
- Estomac
- Intestin
- Peau
- Poumons
- Ovaires
- Œsophage
- Leucémie
- Lymphome
- Utérus col ou endomètre
- Rein
- Vessie
- Prostate
- Pancréas
- Myélome
- Foie

Autre, lequel :

.....

Précisions diagnostiques (type, stade, etc.)



.....
.....

Année de diagnostic du cancer :

Traitement(s) reçus (plusieurs réponses possibles):

- Chirurgie
- Chimiothérapie traditionnelle (cycles)
- Traitement anticancéreux ciblé
- Radiothérapie
- Traitement hormonal/ préventif

Autre, lequel :

.....

Traitements **actuellement** en cours (préciser ensuite dans la table):

- Chirurgie
- Chimiothérapie traditionnelle (cycles)
- Traitement anticancéreux ciblé
- Radiothérapie
- Traitement hormonal/ préventif

Autre, lequel :

.....

Traitement(s) anticancéreux en cours :

Substance (DCI)	Dose	Voie d'admin.	Date Initiation	Dernière dose (DD)/ Prochaine dose (PD)	Date d'arrêt*
<i>Ex. tamoxifène</i>	<i>20 mg 1x/j</i>	<i>po</i>	<i>Avril 2012</i>	<i>En cours</i>	<i>?</i>

*si connu



SUPPLEMENTARY QUESTIONNAIRE S2

QUESTIONNAIRE

STUDY ON THE USE OF COMPLEMENTARY MEDICINE IN ONCOLOGY

Study identification N° (e.g. 008):

Interview date (DD/MM/YY):

In this questionnaire, the term *complementary medicine* is defined as a broad set of healthcare practices that are not part of a country's own tradition or conventional medicine and are not fully integrated into the dominant healthcare system. This definition is inclusive of other terms such as alternative, parallel, natural or holistic medicine. If you do not know about complementary medicine, some examples can be found under question 12. We are interested in all types of complementary medicine, whether prescribed by a physician, a pharmacist or a therapist, or whether you use them on your own initiative, outside of any recommendation from a healthcare professional.

Questions

28. Age:

29. Sex: male female

30. Origin:

- Europe
- Africa
- Central/South America
- North America
- Asia
- Oceania
- Unknown/stateless
- Unknown (not answered)

31. Education level:

- Primary
- Secondary
- Apprenticeship
- High school, college
- University

32. Do you have additional coverage for complementary medicine included in your health insurance?

- Yes
- No
- I don't know



33. Marital status:

- Single
- Married/civil partnership/widowed
- Divorced/separated
- Unknown (not answered)

34. Have you **at any time in your life** used complementary medicine?

- Yes
- No

If yes, go to question 9. If no, go to question 8.

35. You have never used complementary medicine because (several answers are possible):

- You do not believe in it
- It is too expensive
- You have heard bad comments about it
- You are not interested in it
- You do not know enough about it

Other (specify):

.....

.....

.....

If you have never used complementary medicine, please go on to answer questions 21 and 22 only.

36. Have you used complementary medicine **since your cancer was diagnosed**?

- Yes
- No

37. Are you **currently** using complementary medicine?

- Yes
- No



38. If yes, what complementary medicine(s) are you using? (several answers are possible):

- Acupuncture
- Traditional Chinese medicine (Chinese herbal remedies)
- Ayurveda
- Dietary supplements
(trace elements, vitamins and/or minerals)
- Homeopathy
- Reflexology
- Aromatherapy/essential oils
- Hypnosis
- Meditation
- Naturopathy
- Herbal remedies
- Reiki
- Yoga
- Green tea
- Fish oil

Other (please specify):

.....

39. If you are taking one or several *oral (ingested) or injected* complementary medicine(s), could you mention the trade name(s) or substance(s), the dose(s), and the date(s) at which it/they was/were taken, and the reason for using it/them ?

Substance/ Trade name	Dose	Period(s)/ Dates of use	Indication* (1-5)

*Indication: For what reason are you taking this/these complementary medicine(s)? (several answers are possible)

1. To prevent relapse
2. To improve immune system
3. To treat cancer
4. To attenuate adverse effects of chemotherapy
5. Other (specify):



40. According to you, how does/do the complementary medicine(s) you take exert its/their effect (*reporting in words as expressed by the patient*)

.....
.....
.....
.....

41. Who recommended that you use complementary medicine(s) during cancer treatment?

- Family/friends
- Family physician
- Oncologist
- Pharmacist
- Complementary medicine therapist
- Media (journals, radio, television, Internet)
- Personal choice

Other (please specify):

.....
.....

What is your opinion about the following statements?

42. The complementary medicine(s) I take is/are very effective.

strongly agree agree neither agree nor disagree disagree strongly disagree

43. The complementary medicine(s) I take can have side effects.

strongly agree agree neither agree nor disagree disagree strongly disagree

If yes, which side effects do you most fear?

.....
.....

44. The complementary medicine(s) I take can have a **negative** effect on the cancer treatment.

strongly agree agree neither agree nor disagree disagree strongly disagree

If yes, which negative effect do you most fear?

.....
.....



45. The complementary medicine(s) I take can have a **positive** effect on the cancer treatment.

strongly agree agree neither agree nor disagree disagree strongly disagree

If yes, which main positive effect are you expecting?

.....
.....

46. I am sufficiently informed about the **benefits** of the complementary medicine(s) that I take.

strongly agree agree neither agree nor disagree disagree strongly disagree

47. I am sufficiently informed about the **risks** of the complementary medicine(s) that I take.

strongly agree agree neither agree nor disagree disagree strongly disagree

48. Were you asked if you use complementary medicine(s):

By your oncologist? By a nurse in oncology?

Yes
No

Yes
No

49. Was the use of complementary medicine(s) offered:

By your oncologist? By a nurse in oncology?

Yes
No

Yes
Non

If yes, what complementary medicine(s)?

.....
.....

50. Did you mention the use of complementary medicine(s):

To your oncologist? To a nurse in oncology?

Yes
No

Yes
No



51. If the answer to question 23 is yes, was your oncologist/the nurse in oncology familiar with this therapy?

- Yes
- No
- I don't know

52. If the answer to question 23 is yes, how did he/she react?

- He/she encouraged you to continue complementary medicine(s)
- He/she requested you stop using complementary medicine(s)
- He/she made no recommendation

Other (please specify):

.....
.....

53. If the answer to question 23 is no, why did you not mention using complementary medicine(s)?

- He/she did not ask me
- He/she would not understand
- He/she would not be happy about it
- I forgot to mention it
- It is not important to mention it

Other (please specify):

.....
.....

54. If your oncologist deems it inappropriate to continue taking complementary medicine(s) concomitantly with your cancer treatment, would you go on taking it/them?

- Yes, in all cases
- No, I would easily stop taking it/them
- I would need justifications before I decide whether to stop
- I would only stop if there are serious risks of pursuing it/them

If you wish to add further detail to your answer:

.....
.....
.....
.....



APPENDIX 2: **PATIENT MEDICAL DATA**

Study identification N° (e.g. 008):

Age:

Sex: male female

Weight (kg):

*Current renal function impairment? yes no ?

*Current liver function impairment or elevated liver tests? yes no ?

* Yes: if mentioned in a recent list of diagnoses (<1 year) in the patient's medical record.

No: if organ function was recently (<1 year) specified as normal in the patient's medical record.

?: if no detailed information exists in the medical record, or if the last assessment of organ functions was >1 year ago.

Type of cancer:

- Nose
- Ear and throat
- Brain
- Breast
- Stomach
- Intestine
- Skin
- Lung
- Ovary
- Oesophagus
- Leukaemia
- Lymphoma
- Uterus, cervix or endometrium
- Kidney
- Bladder
- Prostate
- Pancreas
- Myeloma
- Liver

Other, specified:

.....



Diagnostic details (histology type, staging, etc.)

.....
.....

Year of cancer diagnosis:

Treatment(s) dispensed (several answers possible):

- Surgery
- Conventional chemotherapy (cycles)
- Targeted cancer therapy
- Radiotherapy
- Hormonal treatment/preventive therapy

Other, specified:

.....

Currently ongoing cancer therapy (detail in table below):

- Surgery
- Conventional chemotherapy (cycles)
- Targeted cancer therapy
- Radiotherapy
- Hormonal treatment/preventive therapy

Other, specified:

.....

Current ongoing cancer treatment(s):

Substance (DCI)	Dose	Route of administration	Initiation date	Last dose (LD)/next dose (ND)	Date stopped*
<i>e.g. tamoxifen</i>	<i>20 mg 1x/j</i>	<i>po</i>	<i>April 2012</i>	<i>Ongoing</i>	<i>?</i>

*if known

SUPPLEMENTARY DATA S3: ARTICLES SELECTED TO ELABORATE THE TABLE OF POTENTIAL PHARMACOKINETIC INTERACTIONS BETWEEN HERBAL MEDICINES AND ANTINEOPLASTIC AGENTS

A) Articles discussing CM substances recurrently cited as presenting documented or theoretical potential for interaction

1. Ali-Shtayeh MS, Jamous RM, Salameh NM, Jamous RM, Hamadeh AM. Complementary and alternative medicine use among cancer patients in Palestine with special reference to safety-related concerns. *J Ethnopharmacol.* 2016 Jul 1;187:104-22. PubMed PMID: 27125594.
2. Alsanad SM, Howard RL, Williamson EM. An assessment of the impact of herb-drug combinations used by cancer patients. *BMC Complement Altern Med.* 2016 Oct 18;16(1):393. PubMed PMID: 27756298; PubMed Central PMCID: PMC5070090.
3. Alsanad SM, Williamson EM, Howard RL. Cancer patients at risk of herb/food supplement-drug interactions: A systematic review. *Phytother Res.* 2014 Dec;28(12):1749-55. PubMed PMID: 25158128.
4. Andersen MR, Sweet E, Lowe KA, Standish LJ, Drescher CW, Goff BA. Dangerous combinations: Ingestible cam supplement use during chemotherapy in patients with ovarian cancer. *J Altern Complement Med.* 2013 Aug;19(8):714-20. PubMed PMID: 23445210; PubMed Central PMCID: PMC3731675.
5. Awortwe C, Makiwane M, Reuter H, Muller C, Louw J, Rosenkranz B. Critical evaluation of causality assessment of herb-drug interactions in patients. *Br J Clin Pharmacol.* 2018 Apr;84(4):679-93. PubMed PMID: 29363155; PubMed Central PMCID: PMC5867089.
6. Ben-Arye E, Lavie O, Samuels N, et al. Safety of herbal medicine use during chemotherapy in patients with ovarian cancer: A "bedside-to-bench" approach. *Med Oncol.* 2017 Apr;34(4):54. PubMed PMID: 28238155.
7. Ben-Arye E, Samuels N, Goldstein LH, et al. Potential risks associated with traditional herbal medicine use in cancer care: A study of middle eastern oncology health care professionals. *Cancer.* 2016 Feb 15;122(4):598-610. PubMed PMID: 26599199.
8. Berretta M, Della Pepa C, Tralongo P, et al. Use of complementary and alternative medicine (cam) in cancer patients: An italian multicenter survey. *Oncotarget.* 2017 Apr 11;8(15):24401-14. PubMed PMID: 28212560; PubMed Central PMCID: PMC5421857.
9. Bossaer JB, Odle BL. Probable etoposide interaction with echinacea. *J Diet Suppl.* 2012 Jun;9(2):90-5. PubMed PMID: 22607644.
10. Carcelero E, Anglada H, Tuset M, Creus N. Interactions between oral antineoplastic agents and concomitant medication: A systematic review. *Expert Opin Drug Saf.* 2013 May;12(3):403-20. PubMed PMID: 23586848.

11. Collado-Borrell R, Escudero-Vilaplana V, Romero-Jimenez R, Iglesias-Peinado I, Herranz-Alonso A, Sanjurjo-Saez M. Oral antineoplastic agent interactions with medicinal plants and food: An issue to take into account. *J Cancer Res Clin Oncol*. 2016 Nov;142(11):2319-30. PubMed PMID: 27316629.
12. De Smet PA. Health risks of herbal remedies: An update. *Clin Pharmacol Ther*. 2004 Jul;76(1):1-17. PubMed PMID: 15229459.
13. Ernst E. The risk–benefit profile of commonly used herbal therapies: Ginkgo, st. John's wort, ginseng, echinacea, saw palmetto, and kava. *Annals of Internal Medicine*. 2002;136(1):42-53.
14. Firkins R, Eisfeld H, Keinki C, et al. The use of complementary and alternative medicine by patients in routine care and the risk of interactions. *J Cancer Res Clin Oncol*. 2018 Mar;144(3):551-7. PubMed PMID: 29356888.
15. Fujita K-i. Cytochrome p450 and anticancer drugs. *Current Drug Metabolism*. 2006;7(1):23-37.
16. Goey AK, Mooiman KD, Beijnen JH, Schellens JH, Meijerman I. Relevance of in vitro and clinical data for predicting cyp3a4-mediated herb-drug interactions in cancer patients. *Cancer Treat Rev*. 2013 Nov;39(7):773-83. PubMed PMID: 23394826.
17. Gurley BJ. Pharmacokinetic herb-drug interactions (part 1): Origins, mechanisms, and the impact of botanical dietary supplements. *Planta Med*. 2012 Sep;78(13):1478-89. PubMed PMID: 22322396.
18. Haefeli WE, Carls A. Drug interactions with phytotherapeutics in oncology. *Expert Opin Drug Metab Toxicol*. 2014 Mar;10(3):359-77. PubMed PMID: 24387348.
19. Hemalswarya S, Doble M. Potential synergism of natural products in the treatment of cancer. *Phytother Res*. 2006 Apr;20(4):239-49. PubMed PMID: 16557604.
20. Hermann R, von Richter O. Clinical evidence of herbal drugs as perpetrators of pharmacokinetic drug interactions. *Planta Med*. 2012 Sep;78(13):1458-77. PubMed PMID: 22855269.
21. Hierl M, Pfirstinger J, Andreesen R, et al. Complementary and alternative medicine: A clinical study in 1,016 hematology/oncology patients. *Oncology*. 2017;93(3):157-63. PubMed PMID: 28641281.
22. Hubner J, Hanf V. Commonly used methods of complementary medicine in the treatment of breast cancer. *Breast Care (Basel)*. 2013 Oct;8(5):341-7. PubMed PMID: 24415987; PubMed Central PMCID: PMC3861850.
23. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs: An updated systematic review. *Drugs*. 2009 2009/09/01;69(13):1777-98. PubMed PMID: 19719333.

24. Kivisto KT, Kroemer HK, Eichelbaum M. The role of human cytochrome p450 enzymes in the metabolism of anticancer agents: Implications for drug interactions. *Br J Clin Pharmacol.* 1995 Dec;40(6):523-30. PubMed PMID: 8703657; PubMed Central PMCID: PMCPMC1365206.
25. Lee RT, Barbo A, Lopez G, et al. National survey of us oncologists' knowledge, attitudes, and practice patterns regarding herb and supplement use by patients with cancer. *J Clin Oncol.* 2014 Dec 20;32(36):4095-101. PubMed PMID: 25403205; PubMed Central PMCID: PMCPMC4517940.
26. Loquai C, Schmidtmann I, Garzarolli M, et al. Interactions from complementary and alternative medicine in patients with melanoma. *Melanoma Res.* 2017 Jun;27(3):238-42. PubMed PMID: 28252553.
27. McCune JS, Hatfield AJ, Blackburn AA, Leith PO, Livingston RB, Ellis GK. Potential of chemotherapy-herb interactions in adult cancer patients. *Support Care Cancer.* 2004 Jun;12(6):454-62. PubMed PMID: 14991387.
28. Meijerman I, Beijnen JH, Schellens JH. Herb-drug interactions in oncology: Focus on mechanisms of induction. *Oncologist.* 2006 Jul-Aug;11(7):742-52. PubMed PMID: 16880233.
29. Olaku O, White JD. Herbal therapy use by cancer patients: A literature review on case reports. *Eur J Cancer.* 2011 Mar;47(4):508-14. PubMed PMID: 21185719; PubMed Central PMCID: PMCPMC3057114.
30. Pourroy B, Letellier C, Helvig A, Chanet B, De Crozals F, Alessandra C. Development of a rapid risk evaluation tool for herbs/drugs interactions in cancer patients: A multicentric experience in south of france. *Eur J Cancer Care (Engl).* 2017 Nov;26(6):e12752-n/a. PubMed PMID: 28881077.
31. Ramos-Esquivel A, Viquez-Jaikel Á, Fernández C. Potential drug-drug and herb-drug interactions in patients with cancer: A prospective study of medication surveillance. *Journal of Oncology Practice.* 2017 2017/07/01;13(7):e613-e22.
32. Shi S, Klotz U. Drug interactions with herbal medicines. *Clin Pharmacokinet.* 2012 Feb 1;51(2):77-104. PubMed PMID: 22257149.
33. Sparreboom A, Cox MC, Acharya MR, Figg WD. Herbal remedies in the united states: Potential adverse interactions with anticancer agents. *J Clin Oncol.* 2004 Jun 15;22(12):2489-503. PubMed PMID: 15197212.
34. Spinella M. The importance of pharmacological synergy in psychoactive herbal medicines. *Altern Med Rev.* 2002 Apr;7(2):130-7. PubMed PMID: 11991792.
35. Treasure J. Herbal medicine and cancer: An introductory overview. *Semin Oncol Nurs.* 2005 Aug;21(3):177-83. PubMed PMID: 16092805.
36. Tsai HH, Lin HW, Simon Pickard A, Tsai HY, Mahady GB. Evaluation of documented drug interactions and contraindications associated with herbs and dietary supplements: A systematic literature review. *Int J Clin Pract.* 2012 Nov;66(11):1056-78. PubMed PMID: 23067030.

37. Undevia SD, Gomez-Abuin G, Ratain MJ. Pharmacokinetic variability of anticancer agents. *Nat Rev Cancer*. 2005 Jun;5(6):447-58. PubMed PMID: 15928675.
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SUPPLEMENTARY TABLE S4: REFERENCES USED TO ASSESS THE INTERACTION POTENTIAL OF EACH COMPLEMENTARY MEDICINE PRODUCT

Complementary Medicine	References*
<i>Alium Sativum</i>	1A, 2A, 3A, 4A, 11A, 16A, 18A, 20A, 23A, 28A, 30A, 31A, 32A, 33A, 44A, 10B
<i>Aronia Melanocarpia</i>	30A, 2B, 3B, 17B, 29B
<i>Boswellia spp.</i>	11B
<i>Camelia sinensis</i>	1A, 4A, 5A, 7A, 8A, 11A, 19A, 29A, 30A, 31A, 10B
<i>Cimicifuga racemosa</i>	27A, 33A, 1B
<i>Citrus spp.</i>	8A, 11A, 12A, 35A
<i>Curcuma longa</i>	1A, 5A, 6A, 7A, 8A, 19A, 28A, 30A, 9B
<i>Echinacea spp.</i>	3A, 5A, 8A, 9A, 11A, 13A, 18A, 23A, 28A, 31A, 32A, 33A, 4B
<i>Foeniculum vulgare</i>	1A, 7A, 5B, 28B
<i>Gingko biloba</i>	2A, 3A, 4A, 5A, 7A, 8A, 18A, 20A, 28A, 30A, 31A, 33A, 36A, 38A
<i>Glycyrrhiza glabra</i>	30A, 4B
<i>Glycine max</i>	33A
<i>Hydrastis canadensis</i>	3A, 20A, 32A, 41A, 4B
<i>Hypericum perforatum</i>	2A, 3A, 5A, 7A, 8A, 11A, 13A, 16A, 17A, 18A, 19A, 23A, 27A, 28A, 30A, 32A, 33A, 34A, 36A, 37A, 40A, 44A, 4B
<i>Lycium spp.</i>	5A, 16B, 18B
<i>Matricaria recutita</i>	1A, 5A, 11A, 31A, 4B, 12B, 19B
<i>Mentha piperita</i>	5A, 8B, 19B
<i>Oenothera biennis</i>	15A, 23A, 33A
<i>Panax spp</i>	7A, 11A, 13A, 16A, 18A, 20A, 23A, 27A, 28A, 30A, 32A, 33A, 40A
<i>Piper methysticum</i>	13A, 28A, 32A, 34A
<i>Piper nigrum</i>	27B
<i>Serenoa repens</i>	11A, 13A, 23A, 32A, 33A
<i>Sylibum marianum</i>	3A, 7A, 8A, 16A, 20A, 30A, 32A, 33A, 39A, 44A, 41A, 49A
<i>Valeriana officinalis</i>	3A, 7A, 11A, 31A, 33A, 34A, 40A
<i>Viscum album</i>	3A, 6A, 7A, 14A, 22A, 26A, 29A, 43A, 10B, 20B, 26B, 30B
<i>Vitis vinifera</i>	7A, 31A
<i>Zingiber officinalis</i>	4A, 6A, 7A, 19A, 9B, 15B
Homeopathic treatments & non-herbal systemic complementary medicine (vitamin C, melatonin,...)**	21A, 25A, 42A, 6B, 7B, 13B, 14B, 21B, 22B, 23B, 24B, 25B, 31B
General articles on interactions in oncology	10A, 24A

* see Supplementary Data S3 for references. As and Bs refer to part A and part B of those references

**No pharmacokinetic interaction was detected with these substances