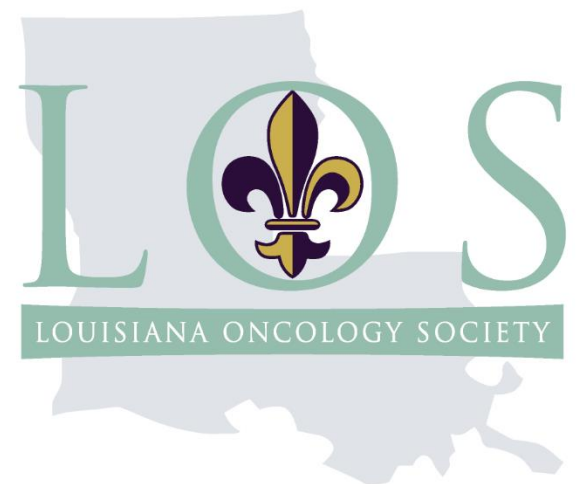


Nutraceuticals in Oncology

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Relevant Financial Disclosures

Enlivity Corporation
-Research Support



Presentation Outline

	<u>Today's Topics</u>
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Timeline >

Background >

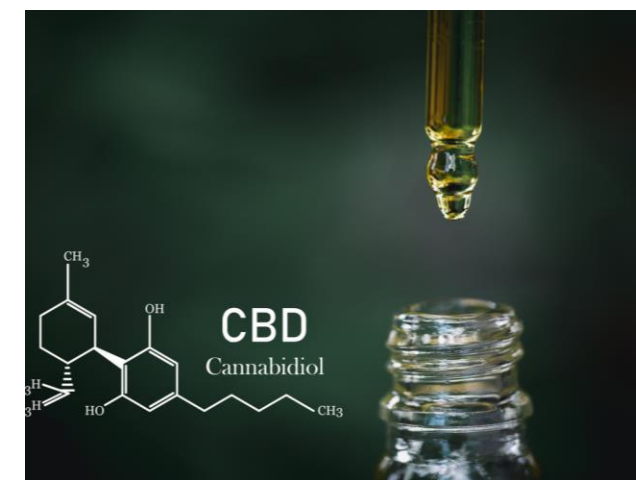
Nutraceutical uses with specific cancer types >

Choosing safe products >

Final thoughts >

References >

Timeline



8000-5000 BCE

Well-established medicinal uses of plants in India and China

1910-1930

Identification of the "vital amine"
Diseases of deficiency that could be treated with food and synthesized vitamins

1920-1950

Isolation and synthesis of all major vitamins
First isolated vitamin was thiamine in 1926

1989

The term 'nutraceutical' was invented in 1989 by Stephen Defelice. Same timeframe when herb drug interactions were first recognized

2021

The global dietary supplements market size was valued at USD 151.9 billion



Nutraceuticals →



Definitions

Products isolated from foods that are generally sold in medicinal forms

A substance, which has physiological benefit or provides protection against chronic diseases

Used to improve health, delay the aging process, prevent chronic diseases, increase life expectancy, or support the structure or function of the body

Mediterranean Diet Pyramid

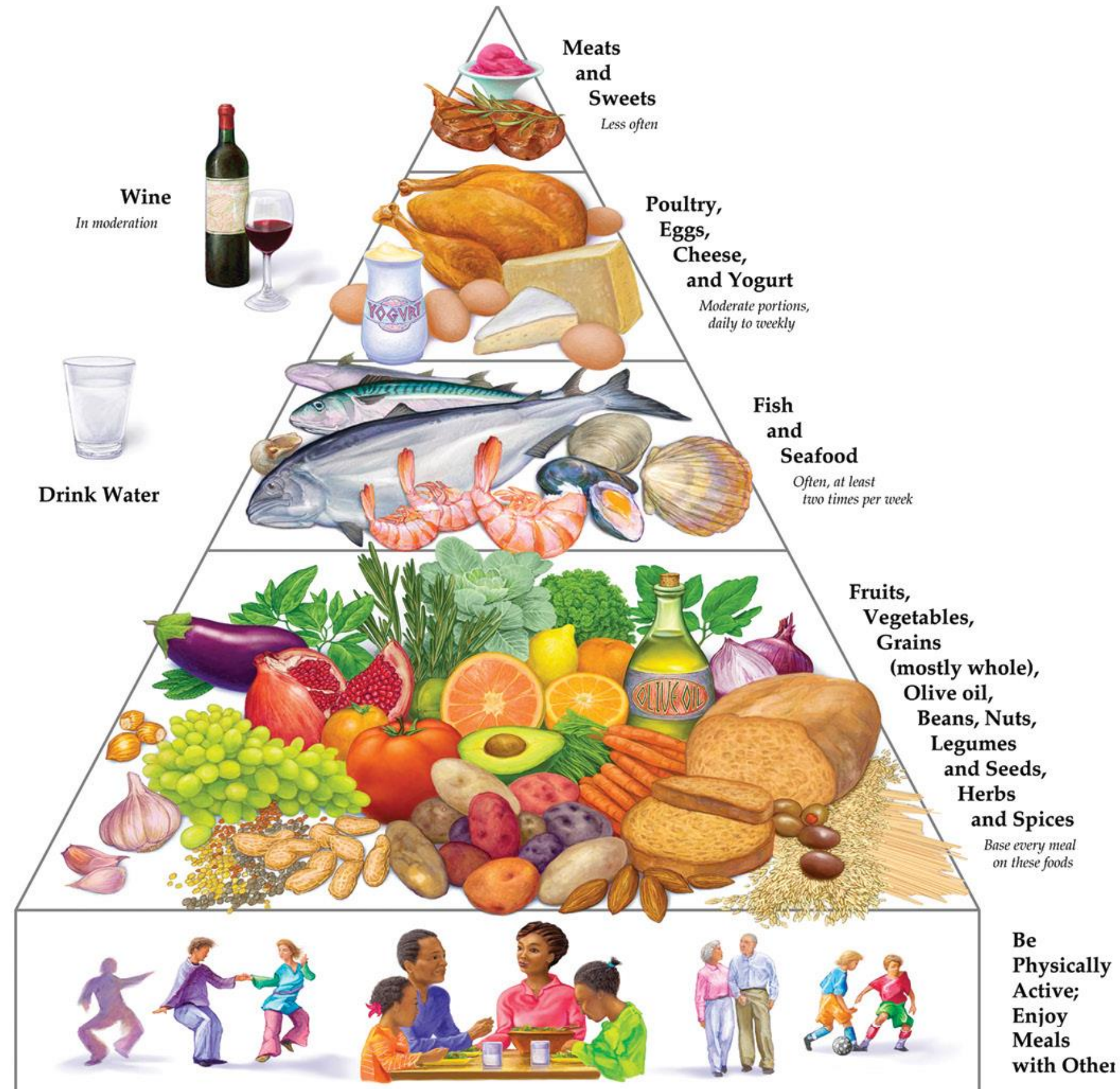


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Food First Approach

Plant-based diets

Change diet patterns and food choices to counteract symptoms of treatment

Support body systems through natural food sources



What if food isn't enough?

Cancer treatment often depletes the body of many nutrients and impairs the ability to eat normally

64% to 81% of cancer survivors report using any vitamin or mineral supplements
26% to 77% reported using any multivitamins

Approximately 50% of US adults use dietary supplements and 33% use multivitamin/multimineral supplements

Velicer CM, Ulrich CM. Vitamin and mineral supplement use among US adults after cancer diagnosis: a systematic review. *J Clin Oncol.* 2008 Feb 1;26(4):665-73. doi: 10.1200/JCO.2007.13.5905. PMID: 18235127.



Lung Cancer

What They are Taking

- No supplements
 - Antioxidants
 - Herbal blends
-

What Might Help

- Vitamin D
 - Probiotics vs fiber supplements
 - Omega-3
 - Turkey tail
 - Multivitamins
-

What Might Harm

- Many herbs
 - Strong antioxidants
 - Immune stimulants
-

Counseling Tips

● ○ ○ Consider the treatment

Gut microbiome seems to be key for immunotherapy response

Probiotics with chemotherapy, fiber with immunotherapy

● ● ○ Consider the stage

Late stage cancer with cachexia

May benefit from fish oil, multivitamin, and more liberalized approaches for alleviating symptoms

● ● ● Dosing Matters

Strong antioxidants may interfere with chemotherapy and radiation, and can potentially increase risk of developing lung cancer for smokers
Examples: Vitamins A, C, E, CoQ10, beta carotene

Multivitamins should not be over about 200% of the established daily value for single nutrients





Hepatocellular Carcinoma

What They are Taking

- Milk thistle
 - “Beef Liver”
 - Jujube
 - Broccoli, alfalfa, dandelion, artichoke extracts (usually in blends)
-

What Might Help

- Branched chain amino acids
 - Fish oil
 - Turmeric
 - Many foods with naturally occurring phytonutrients
-

What Might Harm

- Milk thistle
 - High doses of green teas
-

Counseling Tips

● ○ ○ Improving liver function

High protein, high calorie diets with late evening snack

Branched chain amino acids

● ● ○ Important Foods

Early research shows foods like cruciferous vegetables, pomegranate, garlic, tomatoes, apples as well as spices like ginger and turmeric might be beneficial

Continue to reinforce plant-based diets

● ● ● Supplement Considerations

Appropriate use of supplements like ginger, fish oil, and others with anti-inflammatory properties may help

Overuse of supplements like green tea extracts and milk thistle can be toxic to the liver





Pancreatic Cancer

What They are Taking

- Botanical blends (cinnamon bark, fenugreek, garlic, coriander, bilberry, licorice root, cayenne pepper, etc.)
 - OTC enzyme blends
 - Spirulina
 - Many others
-

What Might Help

- Fat soluble vitamins
 - Omega 3
 - Zinc
 - Vitamin D, A, C, E, or K
-

What Might Harm

- Milk thistle
 - High doses of singular vitamins
 - Herbal supplements from non-reputable sources
-



Other GI Cancers

What They are Taking

- Slippery elm
 - Marshmallow root
 - Licorice root
 - Aloe vera
 - “Lectin defense”
 - Boswellia
-

What Might Help

- Psyllium fibers
 - Probiotics
 - Enteric coated peppermint
 - Glutamine
 - Amino acid blends
 - Ginger
-

What Might Harm

- Garlic
 - Ginkgo
 - Echinacea
 - Ginseng
 - Supplements with caffeine
 - Kava (kava kava)
-

Counseling Tips

● ○ ○ Consider the treatment

Chemotherapy can alter the lining of the gut as well as the gut microbiome

Radiation can irritate the large and small bowel and cause long lasting symptoms

● ● ○ Healing the gut

Several supplements using peppermint, amino acids, and fiber can be safely used during treatment

May reduce symptoms like nausea, diarrhea, mucositis, IBS like symptoms

● ● ● Probiotics

Can be extremely useful in managing GI symptoms but should be used with caution with immunotherapy

If unable to use probiotics, increase fiber intake and natural probiotics --yogurt, kefir, sauerkraut, tempeh, kimchi, miso, pickles, buttermilk, sourdough bread

Soluble fiber is the most useful for diarrhea

-beans, avocado, oats, sweet potatoes, carrots, apples, pears, chia seeds, flax seeds





Breast Cancers

What They are Taking

- Sea moss
 - Black cohosh
 - Ashwagandha
 - Turkey tail/other mushrooms
 - CoQ10
 - Turmeric
 - Many others
-

What Might Help

- Ginger
 - Turmeric from natural sources
 - Omega 3
 - Fiber
 - Calcium and Vitamin D
 - Soy in natural forms
-

What Might Harm

- Black cohosh
 - Red clover
 - Ginko
 - Ginseng
 - Dong quai
 - Licorice
-

Counseling Tips

● ○ ○ The most common cancer

There is the most information (and incorrect information) available for breast cancer patients
Recommendations may vary based on hormone receptor status

● ● ○ When to use supplements

Best time is after surgery, chemotherapy, and/or radiation
Some supplements can be used along side endocrine therapies to help manage side effects

● ● ● Working together

Diet DOES matter

- Manage calorie intake to maintain or lower body weight
- Anti-inflammatory diets can help with muscle and joint pain

Soy in natural forms is NOT bad

- Tofu, tempeh, edamame, soy milk





Glioblastoma

What They are Taking

- Niacin (B3)
 - Curcumin
 - GLA
 - Ginko
 - Cannabis
 - Green tea
-

What Might Help

- Vitamin D
 - Melatonin
 - Cannabis
 - Omega 3
-

What Might Harm

- Vitamin E
 - “Traditional” high fat diets
-

Counseling Tips

● ○ ○ Sativex Trial

Phase II 15 hospital study in UK after promising phase I results
Will recruit more than 200 patients
Combines Sativex (oral spray with THC and CBS) to chemotherapy

● ● ○ Diet Quality

Traditional, obesity-inducing high fat diets associated with more aggressive disease in mouse models

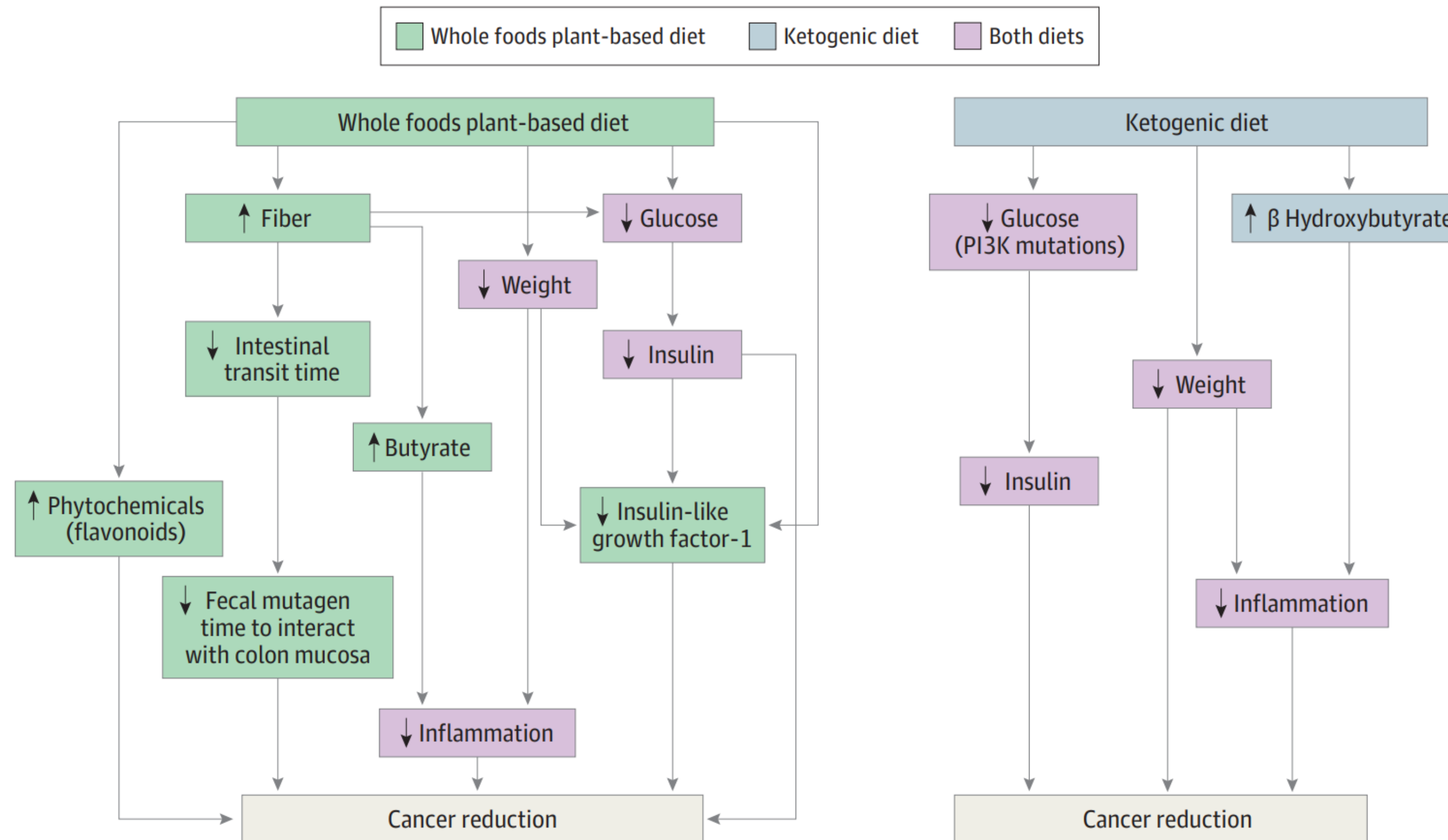
Continue to focus on high quality, whole food plant-based diets

● ● ● Therapeutic ketogenic diets

Traditionally 4:1 fat to carbohydrate and protein
May need to be calorie restricted to be more beneficial
Combination plant-based ketogenic?
Difficult to follow
New tools available like chronometer and keto-mojo
Should be used in combination with traditional therapy



Figure. Association of Plant-Based Diets With Multiple Additional Pathways That Suppress Cancer Growth Compared With Ketogenic Diets

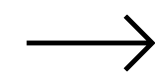


Shah UA, Iyengar NM. Plant-Based and Ketogenic Diets As Diverging Paths to Address Cancer: A Review. *JAMA Oncol.* 2022;8(8):1201–1208. doi:10.1001/jamaoncol.2022.1769



Choosing a Supplement

Making the safest choice



There is an estimated 85,000 + supplements available in the U.S. market

Dietary supplements are regulated as food, not drugs

The FDA is not authorized to review dietary supplement products for safety and effectiveness before they are marketed



Guiding Patients to Safer Choices

01. USE FOOD FIRST

There are no significant risks associated with eating vitamins and herbs as part of a regular diet

Supplemental forms of herbs should be avoided during treatment due to lack of safety information

Vitamins and other nutraceuticals may be used in normal quantities when clinically indicated

02. AVAILABLE CLINICAL RESOURCES

Memorial Sloan Kettering Cancer Center: About Herbs

Natural Medicines Database (requires membership)

Medline Plus (NIH National Library of Medicine)



Guiding Patients to Safer Choices

03. THIRD PARTY TESTING



United States Pharmacopeia (USP)

tests for label accuracy, contaminants, proper bioavailability; made according to FDA Good manufacturing processes

National Sanitation Foundation: NSF/NSF Certified for Sport

tests for label claims, toxicology, presence of contaminants
provides certifications
reviews manufacturing processes

Lab Door- purity and label accuracy testing

buys supplements off retail shelves
provides grades and rankings but not endorsements

Consumer Lab- purity and quality testing

companies pay to be verified
publish lists of "approved" products



Final Thoughts

SUPPLEMENTS CAN HELP

- Help alleviate side effects
- Correct deficiencies
- Support body systems and functions
- Improve tolerance of treatment

DOSING AND TIMING MATTER

- Time of day
- Phase of treatment
- Avoid over and underdosing



References

Pan SY, Litscher G, Gao SH, et al. Historical perspective of traditional indigenous medical practices: the current renaissance and conservation of herbal resources. *Evid Based Complement Alternat Med*. 2014;2014:525340. doi:10.1155/2014/525340

Grand View Research. Dietary Supplements Market Size, Share & Trends Analysis Report By Ingredient (Vitamins, Minerals), By Form, By Application, By End User, By Distribution Channel, By Region, And Segment Forecasts, 2022 - 2030. Pulished March 2022. Accessed 3/20/22. <https://www.grandviewresearch.com/industry-analysis/dietary-supplements-market#:~:text=The%20global%20dietary%20supplements%20market,8.9%25%20from%202022%20to%202030>.

The United States Pharmacopeial Convention. Accessed 3/19/22. <https://www.usp.org/about>

National Sanitation Foundation. Testing, Inspection and Certification. Accessed 3/19/22 <https://www.nsf.org/testing>

Nasri H, Baradaran A, Shirzad H, Rafieian-Kopaei M. New concepts in nutraceuticals as alternative for pharmaceuticals. *Int J Prev Med*. 2014;5(12):1487-1499.

Aronson JK. Defining 'nutraceuticals': neither nutritious nor pharmaceutical. *Br J Clin Pharmacol*. 2017;83(1):8-19. doi:10.1111/bcp.12935

Michels A. What's in the Supplement Bottle? Linus Pauling Institute. Published 02/24/2015. Accessed 03/19/22. <https://blogs.oregonstate.edu/linuspaulinginstitute/2015/02/24/whats-supplement-bottle/>

K. Simon Yeung. Herb-Drug Interactions in Cancer Care. Memorial Sloan Kettering Cancer Center. Published May 2013. Accessed 3/19/22. <https://www.mskcc.org/videos/herb-drug-interactions-care>

Flaig TW, Gustafson DL, Su LJ, Zirrolli JA, Crighton F, Harrison GS, Pierson AS, Agarwal R, Glodé LM. A phase I and pharmacokinetic study of silybin-phytosome in prostate cancer patients. *Invest New Drugs*. 2007 Apr;25(2):139-46. doi: 10.1007/s10637-006-9019-2. Epub 2006 Nov 1. PMID: 17077998.

References

National Library of Medicine. Drugs Herbs and Supplements. Ashwagandha. MedlinePlus. Last reviewed 12/10/21. Accessed 03/12/22. <https://medlineplus.gov/druginfo/natural/953.html>

Li J, Gödecke T, Chen SN, et al. In vitro metabolic interactions between black cohosh (*Cimicifuga racemosa*) and tamoxifen via inhibition of cytochromes P450 2D6 and 3A4 [published online ahead of print, 2011 Aug 9]. *Xenobiotica*. 2011;10.3109/00498254.2011.603385. doi:10.3109/00498254.2011.603385

Montbriand, M. (2004). Herbs or Natural Products that Increase Cancer Growth or Recurrence. *Oncology Nursing Forum*. 31(5)

Davis-Yadley AH, Malafa MP. Vitamins in pancreatic cancer: a review of underlying mechanisms and future applications. *Adv Nutr*. 2015 Nov 13;6(6):774-802. doi: 10.3945/an.115.009456. PMID: 26567201; PMCID: PMC4642423.

Chandler PD, Chen WY, Ajala ON, et al. Effect of Vitamin D3 Supplements on Development of Advanced Cancer: A Secondary Analysis of the VITAL Randomized Clinical Trial. *JAMA Netw Open*. 2020;3(11):e2025850. doi:10.1001/jamanetworkopen.2020.25850

Feldman, D., Krishnan, A., Swami, S. et al. The role of vitamin D in reducing cancer risk and progression. *Nat Rev Cancer* 14, 342–357 (2014). <https://doi.org/10.1038/nrc3691>

Murphy RA, Mourtzakis M, Chu QS, Baracos VE, Reiman T, Mazurak VC. Supplementation with fish oil increases first-line chemotherapy efficacy in patients with advanced nonsmall cell lung cancer. *Cancer*. 2011;117(16):3774-3780. doi:10.1002/cncr.25933

Ghoreishi Z, Esfahani A, Djazayeri A, et al. Omega-3 fatty acids are protective against paclitaxel-induced peripheral neuropathy: a randomized double-blind placebo controlled trial. *BMC Cancer*. 2012;12:355. Published 2012 Aug 15. doi:10.1186/1471-2407-12-355

Widmer M, Hanemann CO, Zajicek J. High concentrations of cannabinoids activate apoptosis in human U373MG glioma cells. *J Neurosci Res*. 2008 Nov 1;86(14):3212-20. doi: 10.1002/jnr.21757. PMID: 18615640.

Lo CS, Kiang KM, Leung GK. Anti-tumor effects of vitamin D in glioblastoma: mechanism and therapeutic implications. *Lab Invest*. 2022 Feb;102(2):118-125. doi: 10.1038/s41374-021-00673-8. Epub 2021 Sep 9. PMID: 34504307.

References

Tajiri K, Shimizu Y. Branched-chain amino acids in liver diseases. *Transl Gastroenterol Hepatol*. 2018;3:47. Published 2018 Jul 30. doi:10.21037/tgh.2018.07.06

Zhou Y, Li Y, Zhou T, Zheng J, Li S, Li HB. Dietary Natural Products for Prevention and Treatment of Liver Cancer. *Nutrients*. 2016 Mar 10;8(3):156. doi: 10.3390/nu8030156. PMID: 26978396; PMCID: PMC4808884.

Freitas RDS, Campos MM. Protective Effects of Omega-3 Fatty Acids in Cancer-Related Complications. *Nutrients*. 2019;11(5):945. Published 2019 Apr 26. doi:10.3390/nu11050945

Montecillo-Aguado M, Tirado-Rodriguez B, Tong Z, Vega OM, Morales-Martínez M, Abkenari S, Pedraza-Chaverri J, Huerta-Yepez S. Importance of the Role of ω -3 and ω -6 Polyunsaturated Fatty Acids in the Progression of Brain Cancer. *Brain Sci*. 2020 Jun 17;10(6):381. doi: 10.3390/brainsci10060381. PMID: 32560280; PMCID: PMC7349634.

Kim S, Jing K, Shin S, Jeong S, Han S, Oh H, Yoo Y, Han J, Jeon Y, Heo J, Heo J, et al: ω 3-polyunsaturated fatty acids induce cell death through apoptosis and autophagy in glioblastoma cells: In vitro and in vivo. *Oncol Rep* 39: 239-246, 2018

Moretti E, Favero G, Rodella LF, Rezzani R. Melatonin's Antineoplastic Potential Against Glioblastoma. *Cells*. 2020 Mar 3;9(3):599. doi: 10.3390/cells9030599. PMID: 32138190; PMCID: PMC7140435.

López-Valero I, Saiz-Ladera C, Torres S, Hernández-Tiedra S, García-Taboada E, Rodríguez-Fornés F, Barba M, Dávila D, Salvador-Tormo N, Guzmán M, Sepúlveda JM, Sánchez-Gómez P, Lorente M, Velasco G. Targeting Glioma Initiating Cells with A combined therapy of cannabinoids and temozolomide. *Biochem Pharmacol*. 2018 Nov;157:266-274. doi: 10.1016/j.bcp.2018.09.007. Epub 2018 Sep 7. PMID: 30195736.

US Food & Drug Administration. What you need to know about dietary supplements. Reviewed 02/17/2022. Accessed 03/19/2022. <https://www.fda.gov/food/buy-store-serve-safe-food/what-you-need-know-about-dietary-supplements>

Fasinu P, Bouic P, Rosenkranz B. An overview of the evidence and mechanisms of herb–drug interactions. *Front. Pharmacol.*, 30 April 2012 | <https://doi.org/10.3389/fphar.2012.00069>

Ambrosone CB, Zirpoli GR, Hutson AD, et al. Dietary Supplement Use During Chemotherapy and Survival Outcomes of Patients With Breast Cancer Enrolled in a Cooperative Group Clinical Trial (SWOG S0221). *J Clin Oncol*. 2020;38(8):804-814. doi:10.1200/JCO.19.01203

References

Spencer C, et al. Dietary fiber and probiotics influence the gut microbiome and melanoma immunotherapy response. 2021; 374:6575. Published 2021 Dec 28. DOI: 10.1126/science.aaz7015

Middha P, Weinstein SJ, Männistö S, Albanes D, Mondul AM. β -Carotene Supplementation and Lung Cancer Incidence in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study: The Role of Tar and Nicotine. *Nicotine Tob Res.* 2019;21(8):1045-1050. doi:10.1093/ntr/nty115

Daniel J. Silver, Gustavo A. Roversi, Nazmin Bithi, Sabrina Z. Wang, Katie M. Troike, Chase K.A. Neumann, Grace K. Ahuja, Ofer Reizes, J. Mark Brown, Christopher Hine, Justin D. Lathia *J Clin Invest.* 2021;131(17):e138276. <https://doi.org/10.1172/JCI138276>.

Twelves, C., Sabel, M., Checketts, D. *et al.* A phase 1b randomised, placebo-controlled trial of nabiximols cannabinoid oromucosal spray with temozolomide in patients with recurrent glioblastoma. *Br J Cancer* **124**, 1379–1387 (2021). <https://doi.org/10.1038/s41416-021-01259-3>

Shah UA, Iyengar NM. Plant-Based and Ketogenic Diets As Diverging Paths to Address Cancer: A Review. *JAMA Oncol.* 2022;8(8):1201–1208. doi:10.1001/jamaoncol.2022.1769