Review of: "Effects of Cinnamon on Cancer Prevention and Progression"

Manuela Cassotta

Potential competing interests: No potential competing interests to declare.

The authors investigate the potential of cinnamon and its bioactive components in cancer prevention and treatment. The manuscript is well-written and addresses a timely topic. However, some key improvements are warranted:

1. Limitations of Animal Models and the Potential of New Approach Methods:

Animal models frequently yield results that poorly translate to human physiology and disease, including cancer, inflammation, microbiota, and ADMET processes (absorption, distribution, metabolism, excretion, and toxicity). (See e.g. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7652903/ , https://pubmed.ncbi.nlm.nih.gov/23401516/ , https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902221/ , https://onlinelibrary.wiley.com/doi/10.1002/fft2.369 , https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7185927/) While the authors cite human studies, they rely heavily on animal data for general claims. The limitations of animal models should be explicitly addressed whenever such data is presented.

Similarly, traditional in vitro studies using static, 2D monocultures or immortalized cell lines have significant limitations. This should also be acknowledged. The manuscript should incorporate studies that utilize human-derived models and relevant new approach methodologies (NAMs) like organoids and organ-on-a-chip systems (e.g. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3790571/).

2. Reframing the Conclusion:

The authors propose further animal studies potentially leading to clinical trials. Instead, they should emphasize the limitations of traditional models and advocate for studies using human-based and human-relevant settings, highlighting the potential of NAMs.

Organoids, organ-on-chip systems, omics technologies, and advanced imaging techniques offer exceptional promise for studying the effects of bioactive compounds on human cancer. These NAMs can evaluate the efficacy and toxicity of candidate drugs with unprecedented accuracy in a human-relevant context, also facilitating non-invasive human in vivo studies.

Some examples of NAMs:

Organoids: https://pubmed.ncbi.nlm.nih.gov/37164297/, https://doi.org/10.1016/j.tem.2020.02.004 , https://pubmed.ncbi.nlm.nih.gov/37958895/https://pubmed.ncbi.nlm.nih.gov/30920154/ ,

https://pubmed.ncbi.nlm.nih.gov/29224780/ , https://pubmed.ncbi.nlm.nih.gov/33092060/ , https://pubmed.ncbi.nlm.nih.gov/37108283/ , https://www.sciencedirect.com/science/article/abs/pii/S0753332205800654?via%3Dihub , https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8215814/

Organs-on-chip: https://www.nature.com/articles/s43856-022-00209-1 (liver-chip for safer preclinical toxicity studies) https://www.sciencedirect.com/science/article/pii/S2666102021000094 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10483668/ (nutraceuticals), https://onlinelibrary.wiley.com/doi/full/10.1002/advs.202002030 …

Other technologies:

https://pubmed.ncbi.nlm.nih.gov/38091344/ , https://doi.org/10.1186/s40246-022-00388-x, https://doi.org/10.1016/j.trac.2017.06.004, https://doi.org/10.31557/apjcb.2022.7.2.133-141 (omics technologies), https://doi.org/10.1093/bib/bby043 , https://doi.org/10.1039/C3FO60184F (in silico clinical trials), https://pubmed.ncbi.nlm.nih.gov/32901140/ (microdosing in phase 0)

3. Summarizing Bioactive Components:

For clarity, consider incorporating a table summarizing the cinnamon bioactive components, their potential effects on specific cancer pathways, and focusing on human-based studies whenever possible.