December 2016 notes on XN,

I have been able to obtain and post in full PDF format, perhaps the most interesting XN research paper.

This 2012 study discussed PCa suppression at "low doses" [although we will see, "low" is still very high].

http://www.prostatecancertopics.com/files/2012-XN-full-paper.pdf

Unfortunately, male humans do not seem to have an easy way presently to consume this "low dose."

Once again, the promise in food powder publications fail's to be realized due to human dose constraints. Note this quote in the paper's conclusion:

"An initial safety study in rats (48) revealed no toxic side effects of XN when administered at 100 mg/kg body weight per day for extended periods of time. Peak plasma concentrations after a single application of 1,000 mg/kg body weight to female rats were detected after 4 h, reaching 3.1  $\mu$ mol/L (49).

## IC50 in the same study ranges from 5 to 10 µmol/L."

The only identified supplement (Swanson) 50 mg is about \$0.30 per pill in semi-discounted quantity 90. Bulk XN is an expensive research grade material. I don't see how a human can get close to 5 µmol/L.

Just as I eventually concluded that JJ Johnson never gave his mice his dish determined IC50 dose of rosemary actives, and getting human patients to his IC50 Rosemary dose was non-obvious with capsules or with raw leaf powder, we can be sure no IPA beer doses a human anywhere close to a dish IC50 w/XN.

And just as we learned with all the other food powders, we also can't know the % actives from leaf to leaf, from cultivar to cultivar, and actives would cost a fortune acquired as pure food research chemicals. [Per blue text quoted above, 1,000 mg/kg body weight would imply ingestion of many grams of pure XN.]

Also, we have the following from a mouse study showing XN improves memory:

"A human would have to drink 2000 liters of beer a day to reach the xanthohumol levels we used in this research," warned Magnussun.

It is SO valuable to find this info on mouse-to-man dose equivalents which shortcuts more study of XN:

Xanthohumol is found naturally in hops and beer, but the highest level used in this research was 60 milligrams per kilogram of body weight per day [in the mice].

This corresponds to a human equivalent dose of **350 milligrams per day for a 70-kilogram person**, which far exceeds any amount that could be obtained by ordinary dietary intake. A level that high would equate to a beer intake of 3,500 pints per day for a human adult. **[so it looks like XN is 0.1mg/pint]** However, that amount of xanthohumol could readily be obtained in a dietary supplement which could be taken once a day. [This text was extracted from the following publication:]

 $\underline{\text{http://oregonstate.edu/ua/ncs/archives/2016/apr/xanthohumol-lab-tests-lowers-cholesterol-blood-sugar-and-weight-gain}$ 

Finally, we have this paper where they study not cytotoxicity [studied elsewhere above 2 micro molar], but realistic activity using sub-micro-molar concentrations, active via other pathways [cytoprotection].

http://www.prostatecancertopics.com/files/XN-2015-ACS.pdf

Here is the only source I have found that could supply this much lower level. Unfortunately, each 50 mg "hops extract" capsule is only 10% XN so only 5 mg / cap. With 5 mg / cap at \$0.22 / cap, this maps to 70 caps / day, \$15.50 per day to achieve 350 mg/day, supposedly giving 60 mg/kg body weight.

http://www.swansonvitamins.com/swanson-ultra-xanthovital-standardized-hop-extract-50-mg-90-veg-caps?CAWELAID=1616678924&SourceCode=INTL417AF&gclid=CKv4hP6u59ACFZE6gQodPaIJrA

It is worth pointing out that the *actual* hops chemical content in IPA, as originally formulated, was fully *successful in* stopping the ale from spoiling on the long ocean voyages to India. Thus, there is evidence that *biologic* growth suppression is in fact achieved, with regard to bacteria and fungi, in the ale at least.

So, just as with rosemary's multiple actives, the XN in hops may not be the only active chemical agent. It may be a mix of active compounds in hops that is virtuous, perhaps even at the ultra-low dose in IPA. This dramatically complicates possible utility and study considering the vast diversity of hops cultivars. There are several brands of "pure dried hops" available in capsules: (w/o assertion regarding XN content). No one in our area has experience with any of these dried total hops products and further issues exist:

- 1. There are downside chemicals in hops in good brewing, XN is retained while others are filtered;
- 2. There are stearate chemicals added to all advertised dried hops capsules just like the rosemary.

https://www.amazon.com/Natures-Way-Flowers-310mg-Capsules/dp/B000Z8YK6C?th=1