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Resveratrol in prostate diseases

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Resveratrol (trans-3, 49, 5-trihydroxys-tilbene) is a polyphenolic antioxidant found in peanuts, grapes and red wine. Preclinical studies indicate that the consumption of food containing resveratrol leads to significant health benefits including possible action of the compound in treating and/or even preventing cancer. One of the long-term epidemiologic studies demonstrated a greater than 50% reduction in breast cancer risk in women taking resveratrol [1]. Furthermore, several *in vitro* studies and experimental cancer models have shown that resveratrol has a potential to suppress the initiation, promotion, and progression of tumors.

Jasiński and co-authors reasonably point out that 'long latency time, make prostate cancer (PCa) an attractive target for chemopreventive interventions [2]. According to Klempner et al., despite only modest clinical evidence of efficacy, complementary and alternative medicine use is common among adults, and recent reports suggest that 25%-50% of PCa patients use at least one of these modalities (mainly: herbal preparations and vitamins) [3]. Therefore, it is necessary to more rigorously evaluate the anticancer properties of the natural compounds.

As described by Jasiński et al., the possible relationship of resveratrol with PCa might be associated with its interactions with androgen regulation. Resveratrol was shown to down-regulate the androgen receptor (AR). Kai and co-authors demonstrated that the combination of resveratrol and the antiandrogen, flutamide, has a synergistic effect on AR inhibition in prostate cancer cells [4]. With the current status of knowledge, the inhibition of the function of the AR seems to be one of the key mechanisms in PCa treatment. According to Iguchi et al., the hydroxyl groups in resveratrol play a key role in their antiandrogenic effect by modulating AR transcriptional activity [5].

However, we should not be that surprised, as suggest Jasiński et al., by the small number of clinical trials with resveratrol. It is quite natural to do many laboratory experiments before commencing human trials. Moreover, there are many more chemical compounds with well-documented anticancer activity awaiting clinical trials. To my knowledge, several phase I and phase II clinical trials are currently underway for resveratrol. I think it is also quite a simplistic approach to explain the French paradox by resveratrol consumption. Firstly, apparently red wine contains very little of resveratrol (inadequate to permit biologic activity in humans) [6]. Secondly, based on the personal observation, I think the French lifestyle together with the healthcare system is much more likely related to the longevity of the French population.

In the review, Jasiński et al., raised one of the most important issues, i.e., the bioavailable amount of resveratrol in humans. Frequently, the concentrations of different agents used in *in vitro* experiments are very different from that achievable in serum.

Unfortunately, despite quoting a huge number of articles, Jasiński et al. do not spend much time on the explanation of the plausible anticancer mechanism of resveratrol. In one of the mentioned publications, Sheth et al. showed that resveratrol reduced the expression of various prostatetumor associated microRNAs (miRs) including miR-21 in androgen-receptor negative and highly aggressive human prostate cancer cells, PC-3M-MM2 [7]. Additionally, resveratrol increased the expression of tumor suppressors, PDCD4 and maspin. According to Sheth and his colleagues, resveratrol's anti-tumor actions in PCa could be explained, at least in part, through inhibition of the Akt/miR-21 signaling pathway.

In my opinion, a key issue is to reveal the predominant *in vitro* mechanism responsible for the anticancer activity of resveratrol. Although the results of many studies are very encouraging, the way from bench to bedside is often very long.

While resveratrol has shown anticancer potential in many experimental studies, it is difficult not to agree with Jasiński et al., that that there is so far insufficient evidence to support the use of the compound for the treatment of PCa patients outside of a clinical trial. There is also not enough clinical data to justify a recommendation for the prophylactic administration of resveratrol.

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References

1. Levi F, Pasche C, Lucchini F, Ghidoni R, Ferraroni M, La Vecchia C. Resveratrol and breast cancer risk. Eur J Cancer Prev. 2005; 14: 139–142.

2. Jasiński M, Jasińska L, Ogrodowczyk M. Resveratrol in prostate diseases – a short review. Cent Eur J Urol. 2013; 66: 144-149.

3. Klempner SJ, Bubley G. Complementary and alternative medicines in prostate cancer: from bench to bedside? Oncologist. 2012; 17: 830–837.

4. Kai L, Levenson AS. Combination of resveratrol and antiandrogen flutamide has syn-ergistic effect on androgen receptor inhibition in prostate cancer cells. Anticancer Res. 2011; 31: 3323–3330.

5. Iguchi K, Toyama T, Ito T, Shakui T, Usui S, Oyama M, Iinuma M, Hirano K. Anti-androgenic activity of resveratrol analogs in prostate cancer LNCaP cells. J Androl. 2012; 33: 1208–1215.

6. Goldberg M, Yan J, Soleasa GJ. Absorption of three wine–related polyphenols in three different matrices by healthy subjects. Clin Biochem. 2003; 36: 79–87.

7. Sheth S, Jajoo S, Kaur T, Mukherjea D, Sheehan K, Rybak LP, Ramkumar V. Resveratrol reduces prostate cancer growth and metastasis by inhibiting the Akt/MicroRNA–21 pathway. PLoS One. 2012; 7: e51655.

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