

## Honey and renal cell carcinoma

Sir,

I read a recent article on honey-induced apoptosis in renal cell carcinoma with great interest.<sup>[1]</sup> Samarghandian *et al.*, concluded that “it prompted us to investigate honey as a potential candidate for renal cancer treatment”.<sup>[1]</sup> I have some discussions on this works. Indeed, honey has been widely studied and mentioned for its usefulness. It is considered as a good natural product that has high antioxidant property. The origin of honey is the flower of. Basically, the insect is the main vector, the bees, carry the nectar and sweet deposits from plants and further modify and collect them in the honeycomb. Within honey, several useful components can be identified, including fructose, glucose, amino acids, vitamins, water, minerals, enzymes, as well as phenolics (which is an important antioxidant). Based on its high antioxidant property, it might have several advantages in prevention against several diseases including intoxication, malignant disease, heart disease, inflammatory disorders, and other degenerative diseases.<sup>[2]</sup> Honey has been widely used in medicine for many centuries. Honey is used in many traditional medical regimens, both Indian and Chinese.

Indeed, there are many useful active ingredients in honey as already mentioned and those ingredients are believed to be the main chemicals that counteract many pathological conditions. Based on the enrichment in phenolic compounds, honey might be useful in cancer management. The antiproliferative effect of honey is well mentioned in the literature.<sup>[3]</sup> Several phenolic compounds in honey such as caffeic acid, caffeic acid phenyl esters, Chrysin, Galangin, Quercetin, Kaempferol, Acacetin, Pinocembrin, Pinobanksin, and Apigenin are widely studied for their application in cancer therapy. For example, Chrysin is reported to have a good antitumorogenic property and effectively suppressed melanoma cells.<sup>[4]</sup> Conclusively, honey is a natural product additive for cancer treatment based on its good cellular growth suppression property. On the other hand, the angiogenesis activity of honey is also mentioned.<sup>[5]</sup> As Samarghandian *et al.*, noted, there are also many reports indicating the enhancement of cell growth effects by honey.<sup>[6,7]</sup> Honey is a classical local regimen for promotion of wound healing. Hence, there is no doubt that honey can stimulate the rapid growth of cell.

It needs further studies to verify the exact effect of honey

on carcinogenesis. Of interest, Samarghandian *et al.*, mentioned that “The proliferative effect of honey on tumor cells was suggested to be a nutritional effect rather than a carcinogenic effect and the antitumor effect was reported to result from many activities, such as the inhibition of DNA synthesis with no signs of cytotoxicity and downregulation of MMP-2 and MMP-9.”<sup>[1]</sup> The question remains as to how we can ensure this proposed concept. What are the factors determining nutritional or carcinogenic effects? Indeed, it could be either promoting of cell growth or suppressing of cell growth by honey, could be possible and expected at the same time. Hence, it is required to know the exact honey induced biological process that can result in desired antitumorogenic property, instead of angiogenesis property, in cancer treatment.

Focusing on the present work, the result might imply the antitumorogenic property. However, this work is not an *in vivo* but an *in vitro* study. The study on cell line cannot warrant the same result in the human body where there are many confounding physiological factors. In addition, although honey is confirmed safe and does not induce hyperglycemia it does not mean that there will be no undesirable effect. The pharmacokinetic and pharmacodynamic properties of honey should be studied well. In a recent report, it was proved that honey can induce CYP3A4 enzyme activity.<sup>[8]</sup> Hence, there is no doubt that honey might have drug interaction in cancerous patients who take several drugs. As a good example, vinblastine which is presently an alternative anticancer drug for renal cell carcinoma also induces CYP3A4 enzyme activity,<sup>[9]</sup> hence, there is no doubt that there can be drug interaction that might lead to failure of treatment. Also, another simple question to be asked in case honey has actual advantages is how to deliver honey to the cancer cell bypassing human metabolism in the digestion and absorption process.

Finally, it should be kept in mind that honey is not a single chemical. In natural acquired honey, the problem of impurity should be mentioned. Many heavy metals such as lead, cadmium, copper, chromium, cobalt, nickel, manganese and zinc are reported contaminate naturally acquired honey.<sup>[10,11]</sup> Those heavy metals have no advantage in cancer treatment but they might be the chemicals that deteriorate the cancer.

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