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# The Janus Corner

## Looking Back  Looking Forward

This occasional section within the journal surveys visions and achievements, often not on the main track of the developing biomedical sciences, but all relating to discoveries and developments of medicinals – both ancient and modern. What they have in common, in one way or another, is providing further background and glances around the edges of the core discipline of pharmacognosy, as it has been and continues to evolve within our times.

# The Preventative Effect of Saffron Against Liver Cancer

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A recent study in the journal Hepatology[1] has demonstrated the chemopreventative effect of *Crocus sativus* (saffron) in decreasing hepatocellular cancer (HCC) induced by diethylnitrosamine (DEN) in laboratory rats. This is a significant finding as HCC is one of the most prevalent cancers worldwide in humans. HCC is of particular concern for individuals suffering from hepatitis B or C, those with iron overload (such as in haemochromatosis) or with fatty liver disease. Alcohol abuse, cigarette smoking and exposure to carcinogens in some cosmetics and foods may also increase the incidence of HCC. The study showed that saffron has dual effects, blocking cellular proliferation, and stimulating apoptosis. Specifically, saffron pretreatment was found to block the elevation of γ-glutamyl transpeptidase, alanine amino transferase and α-fetoprotein, each of which indicate hepatic damage. Saffron pre-treatment also decreased the levels of factors involved in tumor progression including Ki-67, cyclooxygenase 2, nitric oxide synthase, nuclear factor Kappa Bp65 and phosphorylated tumor necrosis factor receptor in DEN treated rats, in comparison to rats not receiving saffron pretreatment. This study was inspired by previous studies that have demonstrated antioxidant[2] and anti-inflammatory[3] properties of saffron which indicated its potential as a potential anticancer agent. The research team is continuing its studies to determine the anticancer mechanism of saffron in preventing HCC.

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## Cyanobacterial Toxins as Targets for Anticancer Therapy

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The control and eradication of cyanobacterial blooms has long been a goal of environmental scientists and those involved with water quality control due to the range of toxins which can be produced by some cyanobacteria. Some of these toxins may produce irritating effects such as "swimmers rash" whilst other cyanobacterial species produce more serious toxins, some of which may be lethal in humans (eg saxotoxin produced by Anabaena spp. and microcystins produced by Microcystis spp.).[1] However, the potential of toxins for therapeutic purposes is also well known. Indeed, drugs have often been described as toxins used at therapeutic doses and toxicity has been used as an indicator of medicinal potential in many previous drug discovery studies. Therefore, it is not entirely surprising that medicinally important properties linked to a cyanobacterial toxin have recently been demonstrated. It was recently reported that one cyanobacterial family (Symploca) secretes a toxin (largazole) with anti-tumor activity against colon, bone and breast cancer cells.[2] In contrast, largazole, had little effect in normal cell lines. This group has also undertaken in vivo studies in mice induced to produce colorectal tumors, demonstrating the ability of largazole to slow tumor progression. Further studies have identified inhibition of ubiquitin activating enzyme (E1) as a probable mechanism for the anticancer activity of largazole.[3] The example of largazole shows the potential of toxins in the treatment of disease states such as cancer. It also indicates the potential of a source of natural drugs that has been largely overlooked previously – those from aquatic organisms.

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