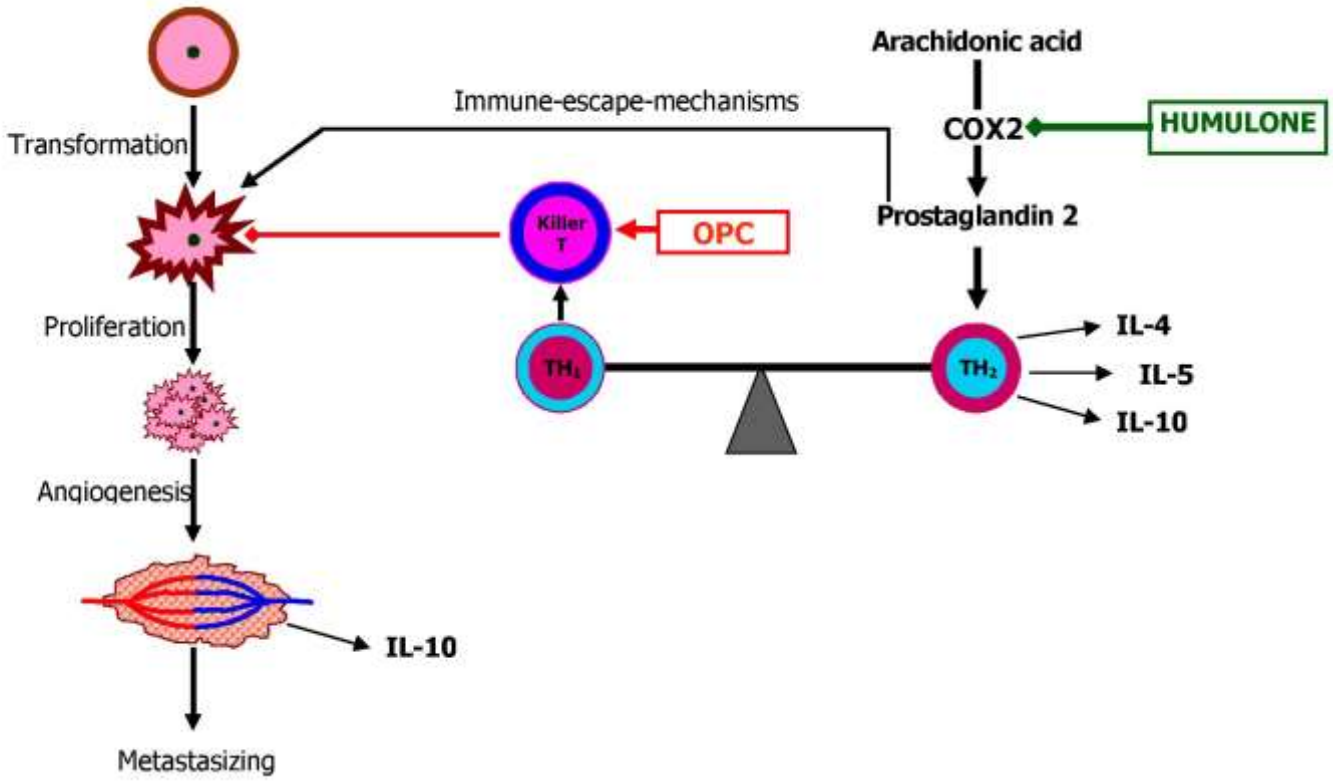
VCW®

Promotion of the Ability to Eliminate Tumour Cells

Importance of apoptosis for prevention and support of cancer therapies

Constantly all tissues are renewed by cell division. In this big quantity of divisions daily there is always a certain amount of faults. This part can increase by external damages (like tobacco). Therefore the body needs mechanism to eliminate these cells avoiding inflammatory reactions if possible. This is performed by a programmed suicide of the cell, apoptosis. If apoptosis is smaller than the number of new formed aberrant cells, tumours can result. There are little differences between normal and defective cells, so that the body can recognize them as strange and eliminate them by immune reaction. These differences in surface antigens are small however and tumour cells can develop mechanisms to escape an immunological attack. The ability of the immune system to eliminate tumour cells is limited therefore. Prostaglandins promote immune-escape-mechanisms and even an immune suppression (Cook 2002; Thun et al. 1993; Marnett 1992; Liu et al. 2001).

The life cycle of tumours starts with a normal cell being transformed to a tumour cell. If this cell can not be eliminated it starts to divide until the tumour reaches a size of 0.5 to 2 mm diameter. The tumour is supplied by surrounding blood vessels and can stay at this size for years. Its growth is limited. But it also can start to form its own blood vessels (angiogenesis) and can grow to a dangerous size. Finally it can separate tumour cells to the blood system. They can settle in other parts of the body as metastases.



Classical treatment of tumours means surgical removal and/or radiation using ionizing rays followed by cytostatics to inhibit cell growth.

Until angiogenesis it is useful to use remedies starting or supporting apoptosis of cells. The same is possible in bigger tumours after removal and during or after chemotherapy as a supplement. Some anti tumour substances point in this direction like alcylating substances (cis-patin and 3-bis(2-chloroethyl)-1-nitrosoharnstoff (BCNU) (D'Amico, McKenna 1994), the topoisomerase inhibitor etoposid (Kaufman et al. 1993), tumour necrosis factor (TNF) (Shih, Stutman 1996), taxol (Gibb et al. 1997) and N-substituted benzamide like metochlopramid and 3-chloroprocainamid (Pero et al. 1997).
But also some natural substances (Dorai, Aggarwal 2004, Taraphdar et al. 2001) from turmeric (curcumin), garlic (diallylsulfide), ginger (6-gingerol) and others are able to promote apoptosis. Therefore they can be used for prevention as well as for complementary curing.

Composition of VCW®

The food supplement combines two active ingredients of plant origin. This is humulone the bitter from hops and oligomeric procyanidine (OPC) from grape seeds or cocoa on nano carriers. Carriers are a drug delivery system, enabling to use very small quantities of active ingredients. Particles are taken up in M-cells of Payer's Plaques directly in monocytes and be transported to their point of operation, without distributing systemically unnecessary quantities in the whole body. Unwanted side effects can be reduced drastically thereby or be eliminated.

Humulone acts specifically as an inhibitor of cyclooxygenase-2 (COX-2) (Honma et al. 1998). It also inhibits angiogenesis of tumours (Shimamura et al. 2001). OPC inhibites lipoxygenase (LOX) (Holzhutter et al. 1997). Both enzymes play pivotal roles in eicosanoide metabolism. This metabolism starts by release of arachidonic acid from the lipid layer of cell membranes. By COX it is transformed to prostaglandines, by LOX to leukotrienes. Both groups of mediators are highly important for tumours, for apoptosis as well as for cellular immune response.
The effect of humulone and OPC is enhanced by combination with an oligounronic acid complex (from seaweed). It is able to transfer catalytically (as phase transfer catalyst) oxygen to cells.

Impact of VCW® on immune response

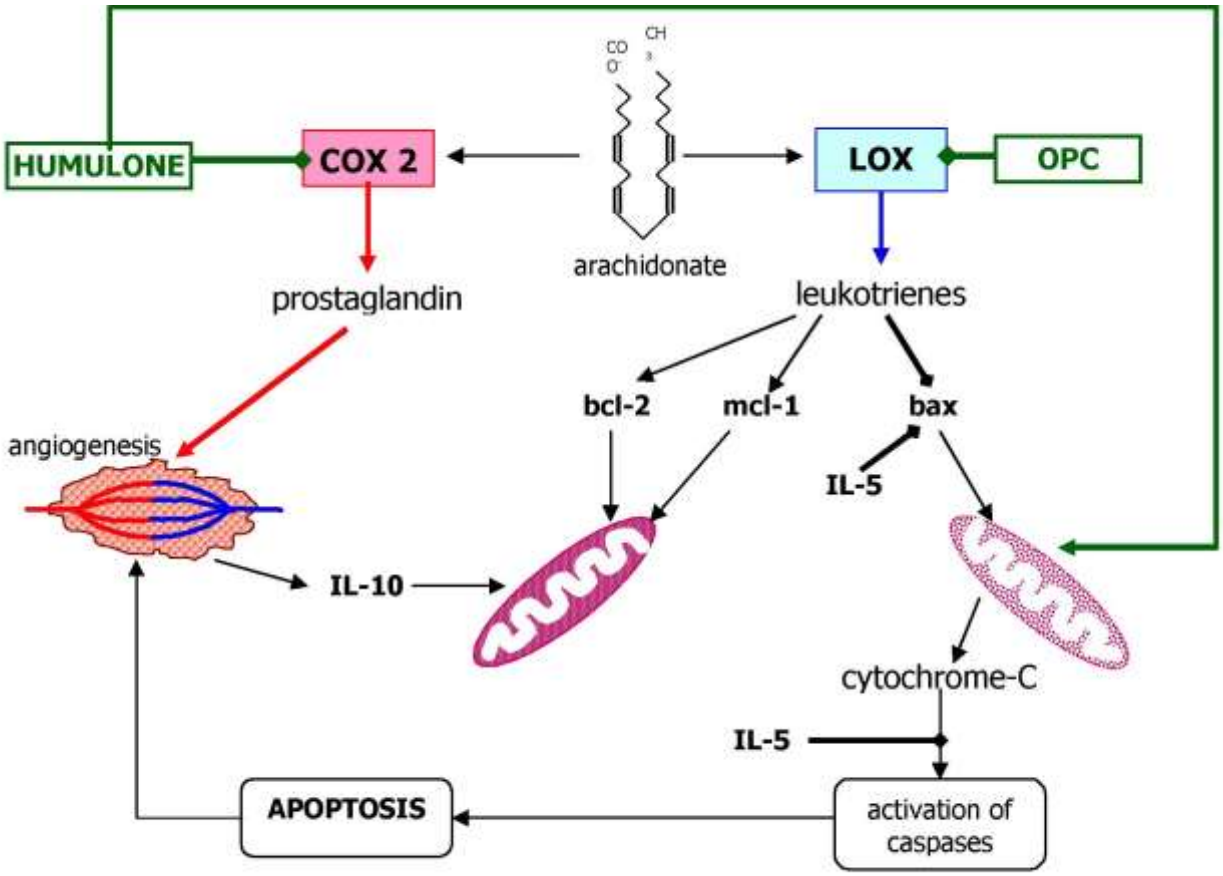
Prostaglandins promote humoral TH2-modulated immune response (Honma et al. 1998; Shinamura et al. 2001). Procyanidines enhance cellular immune response in effector cells (T-killer cells) (Malina et al. 2000). Cellular immune response is mainly responsible for the elimination of transformed and tumour cells. Simultaneously with TH1-modulation cytokines IL-5, IL4 and IL-10 are down regulated. They play a very important role by inhibiting apoptosis. Many sorts of tumours are associated with high concentrations of IL-10 [malignant melanoma (Dummer et al. 1995; Sato et al. 1996), ovary tumour (Gotlieb et al. 1992), other tumours (Fortis et al. 1996; Wittke et al. 1999), lymphomas and myelomas (Khatri & Caligiari 1998; Klein et al. 1999)]. IL-10 inhibits apoptosis by reducing permeability of mitochondrial membrane (Perianayagam et al. 2005).

Impact of VCW® on apoptosis

For the most part apoptosis is determined by permeability of mitochondrial membrane for cytochrome C. A high permeability means a big release of cytochrome C to cell plasma. It activates a cascade of caspases, enzymes that fragmentise the nucleus first and prepare parts of cytoplasm (apoptotic bodies) to be eliminated finally by phagocytes.

Permeability of mitochondrial membrane is controled by many mechanisms and substances. The mainly aim of these mechanisms is to protect mitochondrial DNA that is not protected by histones like DNA of nucleus. The mechanisms work by sealing the membrane. One result is that aerobic respiration in mitochondria is replaced by anaerobic fermentation by pentose phosphate shunt (the well known Warburg phenomenon of tumour cells).
Permeability of the membrane is enhanced by humulone (Tobe et al. 1997) as well as by proapoptotic Bax. Bax however is inhibited by IL-5, a cytokine typical for TH2-modulated

immune response (Dewson et al. 2001, Maccarone et al. 1997). It is the same cytokine that inhibits the activation cascade of caspases.
Permeability of mitochondrial membrane is reduced by antiapoptotic bcl-2 and mcl-1. They are activated by leukotrienes (Tong et al 2002). Leukotrienes also inhibit Bax (Tong et al. 2002). Since they are formed from arachidonic acid by lipoxygenase (LOX) they can be reduced by LOX-inhibitor OPC (Holzhutter et al. 1997).
Tumour cells during angiogenesis show a significant over expression of COX-2 enzyme (Subbaramaiah, Dannenberg 2003). A COX-2 inhibitor like humulone can be able to prevent this critical stage and possibly is able to reverse even angiogenesis (Iniguez et al. 2003). In addition in mammary cancer prostaglandins (formed by COX-2) enhance aromatase activity, a source of oestrogen production.



SUMMARY:

VCW® is a combination of humulone (a COX-2 inhibitor), OPC (a LOX-inhibitor) and an immune modulator. This is a possibility to promote apoptosis of tumour cells and an elimination of them by cellular immune response. It can be used for prevention as well as for a complimentary treatment of tumours.
Observations showed, that chemotherapy could be tolerated significantly better by using VCW®.