PRACTITIONER ONLY

Salvestrol: Practitioner Information

Salvestrols were recognised as a new class of phytochemicals, discovered by a team of scientists spearheaded by Professor Gerry Potter and Professor Dan Burke, as part of their work over a 20 year period. This discovery was made as a result of multiple research projects, including the Cancer Discovery Group project at De Montfort University in Leicester. Salvestrols are phytoalexins manufactured within plants as a biochemical defence mechanism against pathogenic attack.

These anticancer micronutrients are found naturally in abundance in specific fruit and vegetable varieties. However, modern farming techniques, for example the use of agrochemicals, have removed the necessity for plants to mount their own internal defence processes and manufacture Salvestrols. Consequently, the Salvestrol levels found in commercial produce are severely depleted in comparison to the levels present in their heritage and organic counterparts.

Once inside the human body Salvestrols become activated within tumour cells after binding to the cytochrome P450 enzyme, CYP1B1 (pronounced “sip one bee one”), which is intrinsic to cancer cells and absent in normal cells. This enzymatic reaction produces metabolites which activate a cascade of chemical reactions that bring about apoptosis (programmed cell death) of the cancerous cell, without harming normal cells [(41)]. Apoptosis is a natural regulatory mechanism utilized during homeostasis to destroy aberrant cells. This natural survival mechanism, developed within the human body over thousands of years, is under-utilized due to the fact that our modern diet has become deficient in Salvestrols.

Salvestrols are highly specific to cancer cells and are harmless to normal cells. This specificity of action is possible due to the fact that CYP1B1 is an innate component of cancer cells and has been shown to occur in all of the wide range of different types of cancer that have been studied to date.

The CYP1B1 enzyme appears to be highly over-expressed in all primary human tumours. A wealth of data exists in the literature which unequivocally demonstrates CYP1B1 to be a universal cancer marker in over 30 independent studies of almost 2000 samples of confirmed cancerous cells, along with what were considered to be normal cells. In the majority of the studies, cancer tissue samples were studied by immunohistochemistry and CYP1B1 was found to be specifically localized to the cancer cells but absent from the surrounding normal cells. This was the case for tissue from the bladder, brain, breast, cervix, colon, oesophagus, kidney, lung, lymph node (i.e. non-Hodgkin’s lymphoma), prostate, ovary, stomach, testis and uterus [1-12], among others [16, 21, 22, 24, 28, 36, 37]. Additionally, since CYP1B1 is expressed in pre-malignant cells, for example colorectal adenomas,[4, 10] lung adenomas,[17] cervical intraepithelial neoplasia,[9] and prostatic intraepithelial neoplasia,[5] it is possible that the CYP1B1 in supposedly normal tissues of cancer patients was in fact being detected in pre-malignant cells.

Collectively, the above information provides the rationale for the use of therapeutic levels of Salvestrols in the treatment of cancerous and pre-cancerous conditions.

For more detailed information on Salvestrols and diet we recommend reading the book by Dr. Brian Schaefer “*Salvestrols, Natures Defence Against Cancer: Linking Diet & Cancer*” (2012).

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Dosage Guidelines

(One capsule = 2,000 Salvestrol points):

Ideally taken first thing in the morning with water or organic fruit juice at least 30-40 minutes before food or other beverages.

Initial Loading dose: 3-6 capsules/day (6,000 – 12,000 points) for 4-6 weeks
Two thirds (⅔) of dose in the morning, remaining third (⅓) 3-4 hours later

Adapt to the individual as needed.

Active Treatment:

- Three (3) capsules/day (6,000 points):

  Two thirds (⅔) of dose in the morning, remaining third (⅓) 3-4 hours later
- If cancer is aggressive/ metastasised / Stage 4, increase morning dose by 1 capsule per day (2,000 points)
- If there is Central Nervous System (CNS)/ Brain involvement, double the dose
- If there is no response after 3 weeks, double the dose
- If there is a concurrent fungal infection increase morning dose by 1 capsule per day (2,000 points)

*Increased risk / Exposure to Inhibitors:

- Exposure to agrochemical inhibitors of CYP1B1 (see Inhibitor section below) - identify source of exposure, including food sources and remove
- If patient is a smoker – strongly encourage cessation of smoking (this is crucial)

Maintenance:

- One (1) capsule/day (2,000 points)

*Increased risk – see above

Preventative (Never diagnosed):

- Three (3) capsules/week (6,000 points)

*Increased risk - see above

Increasing the effectiveness of Salvestrols:

In brief the following are the key factors for increasing the effectiveness of Salvestrols:

- Elimination of Inhibitors
- Appropriate dosing
- Cofactors
- Dietary Change
- Bioavailability
- Exercise
- Monitor Blood Profiles
- Reduce Stress

Elimination of inhibitors

There are a variety of substances that inhibit the operation of the CYP1B1 enzyme; these need to be analysed for each individual. Exposure can come through the workplace, the environment and the home. Chief among these are agrochemicals, especially fungicides which are used in agriculture but are also used elsewhere which makes them difficult to avoid. Fungicides can be used on golf courses, public park areas, in new carpeting, antidandruff shampoos, house paints and cleaning agents used in air conditioning ductwork. **Ketoconazole** (Nizoral, Extina, Xolegel, Kuric), is a known CYP enzyme inhibitor. It is an antifungal compound added to antidandruff shampoos and various antifungal creams.

Herbicides that contain glyphosate are also potent inhibitors of CYP enzymes. Residues can be found on many commercially grown crops. In light of this a systematic look for sources of CYP1B1 inhibition is a very good idea in these situations. Screening the blood for the presence of agrochemicals can be very instructive in this regard.

Dietary inhibitors of CYP1B1 also exist: High doses of Resveratrol (over 50 mg per day); Laetrile or Amygdalin (vitamin B17, from apricot kernels and bitter almond); and Hesperetin and Naringenin (from grapefruits).
http://www.medsafe.govt.nz/profs/PUArticles/March2015FruitInteractions.htm
In addition, artificial sweeteners and preservatives may produce an inhibitory effect. Anecdotal experience has revealed that there are various herbal supplements or products that may inhibit CYP1B1. These include Cannabis, Ginkgo biloba, Ginseng, Hops and St. John's wort.

Smoking, be it cigarettes, pipes or otherwise, produces carbon monoxide which is also a CYP1B1 inhibitor. Carbon monoxide irreversibly binds to the haem iron in the enzyme and thus prevents the metabolism of Salvestrols. This type of inhibition is most relevant for those with lung cancers and cancer of the blood as concentrations of carbon monoxide are likely to be highest concentrations in the lungs and blood stream.

Strive to eliminate or minimise exposure to:

- Agrochemicals (Pesticides, Fungicides, Herbicides)
- Fungicides (topical applications)
- Vitamin B17 (Amygdalin, Laetrile)
- Artificial sweeteners
- High dose (over 50mg per day) Resveratrol
- Carbon monoxide
- Hesperetin and Naringenin (from grapefruit)
- Herbal products such as Ginkgo biloba, Ginseng, Hops and St. John's Wort
- Cannabis use

In the presence of the inhibitors listed above, a higher threshold dose of Salvestrol will be required to effectively compete for the CYP1B1 binding site and achieve beneficial metabolism. In addition, eliminating exposure to inhibitor(s) will improve effectiveness.

Appropriate dosing

Dosing is dependent on the individual and their situation. Factors including age, stage and aggressiveness of the cancer; site of the cancer or metastases; exposure to inhibitors; the presence of concurrent fungal infections; and the speed of the individual's response, all of these factors need to be taken into consideration when determining a dose for ongoing use.

Salvestrols will reach peak concentration in the blood three hours after ingestion. The target blood levels, in order to deliver a therapeutic concentration, is 4µM. Peak concentration of Salvestrol **metabolites** in the blood is realised five hours after ingestion so we can infer that peak concentration in the cancer cells would occur somewhere around four hours after ingestion.

Therefore, to maintain the maximum therapeutic window as long as possible, it is best to provide two thirds (⅔) of the total Salvestrol points at breakfast and the remaining third (⅓), three to four hours later. The second dose will boost blood levels just as the concentration from the first dose is diminishing, to keep the blood levels higher for a longer period of time. This protocol has been found to be more effective than spreading the dose out throughout the day.

When Salvestrols are introduced in therapeutic doses they will be taken up by the body until a steady state is achieved. This is the purpose of the initial loading dose: ongoing research indicates that after achieving a steady state the Salvestrols can begin to target cancer cells. Given this development it is important to achieve a steady state as quickly and efficiently as possible so that the patient can start to benefit from the therapeutic effects.

Concurrent use of Chemotherapy

There are no known interactions between Salvestrols and chemotherapy or radiotherapy treatments. This includes oral, intravenous or implanted forms. It is important to note that Salvestrols are **not** antioxidants, they are phytoalexins (secondary plant metabolites), which are produced by plants as a result of pathogenic attack.

Concurrent fungal infection

In our experience, reported significant fungal infections appear to be common in people at the time of their cancer diagnosis and Salvestrols can be utilised in combating both the fungal infection and cancer cells. Incidentally, Salvestrols are phytoalexins which are produced in plants as antifungal agents.

Side Effects / Contraindications

No known side effects.

Contraindications - concurrent use of: vitamin B17 (amygdalin, laetrile), resveratrol (over 50mg per day), herbal products including Ginkgo biloba, ginseng, hops and St. John's wort, use of cannabis and dietary intake of artificial sweeteners, hesperetin and naringenin (from grapefruit). See above.

Cofactors

A deficiency in any one of the following nutrients has the potential to seriously impair the ability of CYP1B1 to activate Salvestrols and carry out their function.

Biotin (vitamin H)

Biotin is a non-selective inducer of enzymes; it has been shown to stimulate expression of CYP1B1 thus increasing Salvestrol metabolism. Biotin has also been shown to inhibit NFkB, a transcriptional factor that is important in tumour survival. Relatively small amounts of biotin accomplish this.

Niacin (vitamin B3) and Cobalamin (vitamin B12)

Niacin and cobalamin are essential for the Salvestrol activation reaction. This reaction is optimised when the body obtains the sufficient quantities of each nutrient. To achieve the appropriate level of niacin (nicotinamide) and cobalamin a good medium strength, B vitamin complex, product is recommended as this will avoid disequilibrium of other B vitamins in the body.

Magnesium

Magnesium is an essential cofactor for the CYP1B1 enzyme activity thereby facilitating the metabolism of Salvestrols. Research indicates that the activity of CYP1B1 is reduced by 50% when levels of magnesium are inadequate.

Iron

CYP1B1, like other CYP enzymes, utilises iron at its core to oxidise various compounds that enter the body. This is how CYP1B1 metabolises Salvestrols to activate the mechanisms that induce programmed cell death or apoptosis in the diseased cell. Cancer sufferers are often anaemic, a situation that interferes with the biogenesis of rescue enzymes like CYP1B1. Given this, it is important that the body is supplied with sufficient levels of iron either through the diet or supplementation.

Vitamin C

Dietary sources of vitamin C should be included to aid in the absorption of plant sources of iron. Vitamin C also stimulates the immune system to assist the body in getting rid of cell debris resulting from apoptosis. A further benefit of Vitamin C comes from it serving as a sacrificial antioxidant to prevent degradation of Salvestrols in the body.

Unrefined Essential Fatty Acids (EFA)

Cancers of the central nervous system and metastases to the central nervous system benefit from a combination of Salvestrol and unrefined fatty acids. Among other beneficial effects, they assist with transportation from the blood into brain tissue. Independent research has shown the use of unrefined fatty acid supplements (represented by EyeQ and Efalex) yields favourable results.

The use of essential fatty acids (EFA) in combination with Salvestrols is recommended for women with breast and ovarian cancer, unrefined Omega 6 fatty acids; Gamma-linolenic acid (GLA) in particular [47], preferably sourced from high quality evening primrose oil (EPO). However, case studies report that the use of Omega 3 fatty acids, can lead to breast tenderness. Consequently, the use of unrefined EPO is suggested.

There is an established link between endocrine disrupting chemicals including bisphenol-A (BPA), methoxychlor, 2,3,7,8-tetrachlorodibenzo-p-dioxin, phthalates, and genistein and disorders of reproductive tissues in females [45, 46]. Further, research has demonstrated that EFAs will kill human breast carcinoma cells *in vitro* [48]. Again, this supports the use of EFAs in the treatment of breast and reproductive tissue cancers in women.

Dietary Change

Organically grown fruit and vegetables will supply additional Salvestrols along with an abundance of other beneficial nutrients while minimising ingestion of agrochemicals. A switch towards increased organic produce consumption will also bring about beneficial changes in the gut microbiome for increased absorption of nutrients. Analysis has shown that heritage varieties contain higher levels of Salvaetrols,[51] than newer varieties. This would be consistent with the analysis of a Victorian diet compared with a modern diet and lifestyle due to changes in agricultural practises, [52]. Further benefits to nutrient absorption can be obtained from unrefined plant oils and the use of Piperine, a constituent of black pepper and certain long peppers, has been shown to increase the bioavailabiity of dietary nutrients.

Bioavailability

In order to be effective, Salvestrols must be absorbed, conjugated and transported so that they can reach the cancer cells in a bioactive form.

In the gut, plant sugars that are used to transport Salvestrols need to be cleaved or separated from the water-soluble (hydrophilic) Salvestrols by natural gut flora or probiotics before absorption can take place. Frequent use of antibiotics is likely to deplete the natural gut flora that facilitates this natural process. For this reason the use of a broad spectrum probiotic is recommended in order to support absorption.

Once absorbed through the gut wall the Salvestrols need to be readied for transit through the body. For the more hydrophilic Salvestrols a human sugar needs to be re-attached in order for them to be transportable, this process occurs within the liver. Optimal liver function must be addressed when developing a treatment plan.

For the more fat-soluble (lipophilic) Salvestrols a good mix of unrefined fatty acids will assist with their transportation especially when the target cancer is in the brain or central nervous system. A mixture of unrefined Omega 3 and Omega 6 oils can assist with transportation into the fatty tissues.

Exercise/Oxygen

Oxygen supplies electrons to CYP enzymes for the metabolism of substrates. Moreover, recent laboratory studies have shown that an oxygen-rich environment stimulates anti-cancer immune cells, [53]. Modest exercise, breathing exercises or oxygen supplementation, when Salvestrols are at peak concentration in the cancer cells, is the most effective way of supplying these electrons for use in metabolism of Salvestrols. Peak concentration in cancer cells takes place around four hours after ingestion. The peak therapeutic window between peak concentration of Salvestrols in the blood and the peak concentration of the Salvestrol metabolites in the blood is about two hours long.

One illustration of the importance of oxygen in metabolism of Salvestrols by CYP1B1 is that cancers of the lung and blood respond very well to Salvestrols when the environment is rich in oxygen.

Time	Salvestrol use – Oxygen use	Notes
Hour 0	Administer 2/3rd of the daily Salvestrol dose:	
Hour 1		
Hour 2		
Hour 3	Administer the remaining 1/3rd of the daily Salvestrol dose.	Peak Salvestrol concentration in blood
Hour 4	Administer oxygen therapy or have patient engage in light exercise or breathing exercises for 10 minutes.	Peak Salvestrol concentration in cancer cells
Hour 5		Peak Salvestrol metabolite concentration in blood
Hour 6		Peak concentration of second dose of Salvestrols in blood
Hour 7	Administer oxygen therapy or have patient engage in light exercise or breathing exercises for 10 minutes.	Peak concentration of second dose of Salvestrols in cancer cells
Hour 8		Peak concentration of second dose of Salvestrol metabolite in blood

Note: Modest exercise, such as a walking, three to four hours after ingesting Salvestrols. This will help to boost oxygen levels and greatly facilitate beneficial metabolism of Salvestrols. Should the patient be unable to take even modest levels of exercise then other approaches to boosting oxygen levels can be explored:

breathing exercises, the use of bottled-oxygen for short periods of time, and the use of hyperbaric oxygen chambers, are valuable options.

Monitor Blood Profiles

It is important to screen for the presence of various chemicals that are known to inhibit CYP1B1 as effectiveness of Salvestrols will be minimal in the presence of these inhibitors. If these inhibitors are found, a higher dose of Salvestrols will be needed while exposure to the inhibitors in eliminated or reduced and the inhibitors are eliminated from the body. Repeat monitoring should be done until the inhibitors are eliminated.

Stress Management

For decades the deleterious effect of stress on health has been studied, in the past decade there has been a growing body of research looking at the relaxation response. This research shows that through a brief daily practice of yoga, meditation, repetitive prayer, deep breathing exercises, gene expression can be altered in ways that are beneficial for recovery [(44)]. Almost everyone fighting a serious illness suffers from stress.

The relaxation response, once activated, can result in significant improvement in a person's state of mind [(44)]. This response be activated through short, daily periods spent focusing on mindfulness, visualisation, singing and hypnosis.

Also, encourage the patient to track their own progress to recovery through journaling as nothing instils hope like signs of recovery. Get the patient to record and plot symptoms so that they can see improvements as they progress.

Belief is the foundation of the placebo effect and we may as well utilise this power alongside our interventions.

Phytonutrient Activity

Phytonutrients rarely have a single mode of action. We have been focused on the mechanism of action brought about by the metabolism of Salvestrols by CYP1B1 but as our case study participants have repeatedly informed us there appears to be health benefits above and beyond this anticancer mechanism.

Salvestrols have been shown to have anti-inflammatory and other beneficial effects which are not yet understood.
We have had reported relief of pain in cases of breast cancer, colon cancer, anal cancer, Chronic Lymphatic Leukaemia (CLL), and melanoma. A possible explanation may be that once a cancer starts to shrink the pressure on surrounding tissue is diminished with consequent relief of pain; coupled with the reported anti-inflammatory effects and reduction of swelling.

Other reported beneficial effects have been identified in patients suffering from osteo-arthritis, Type II Diabetes, cardiovascular conditions, and benign prostatic hyperplasia (BPH).

At Salvacare we continue to document these reported benefits and aim to further pursue research and development in these areas.

Monitoring patient progress -

Addressing a slow or non-existent response

Response to any intervention varies from one individual to another. We have those that respond quickly, slowly, at low doses, at higher doses, and some who don't seem to respond at all.

An important factor that we have to acknowledge is that a large number of people do not consider natural medicine, dietary change and nutritional approaches until all conventional medical options have been exhausted, it is their last resort. In these situations, at the point of initial contact the individual is often very ill, the body is not working optimally and there is very little time left for any approach to return the person to good health.

In order to identify potential problems we must consider the processes which need to occur subsequent to Salvestrol ingestion; they must be absorbed, conjugated and transported to the cancer cells, thus bioavailability is crucial. They then have to enter the cancer cell and be metabolised by CYP1B1 to produce a metabolite that will initiate apoptosis. During this process, with a person in poor health any number of these mechanisms can be compromised any of which may be responsible for a poor response.

To reverse a slow or non-existent response the key factors may need to be re-visited:

Elimination of inhibitors, appropriate dosing, cofactors**,** dietary change, bioavailability, reduction of stress and exercise/oxygen.

Note: A number of physicians in Germany take the following approach: if the patient is not showing any response or is responding very slowly, three weeks after they should have reached a steady state of Salvestrol levels, (7-9 weeks after treatment has commenced), the dose should be doubled. The theory behind this is that if there is competition for the CYP1B1 binding site from other compounds, (also known as competitive inhibition), an increase in the relative concentration of Salvestrols will result in more of the Salvestrols being metabolised.

Managing Remission

Once a patient has reached remission our research shows that remaining in remission is dependant upon patient compliance with continued Salvestrol use and dietary change. Adjust the dose of Salvestrols to reflect their remission and encourage continued dietary change along with beneficial lifestyle change to ensure that the cancer remains in remission. If patient compliance is poor and the cancer returns, the treatment program must be re-initiated.

Final comment

Finally, when the patient is feeling like their recovery is too slow, and you have worked through all of the above, remind the patient that we have a case study of a gentleman with prostate cancer where is took 18 months before he was told he was clear of the disease. At time of writing, he has now been clear of this disease with no recurrence for 7 years! Some people will simply take longer to reach remission than others.

Salvestrol: Practitioner Information

Summary:

- Investigate patient exposure to CYP1B1 inhibitors and avoid: laetrile, resveratrol, hesperetin, naringenin, fungicides, herbicides.
- Check for deficiency in magnesium, niacin, cobalamin and iron. Remedy with a good multivitamin.
- Check the state of gut flora. Remedy with a broad spectrum probiotic.
- Check liver function for making plant nutrients bioavailable. Consider supplementing the diet with piperine.
- Check the dietary mix for fatty acids. Remedy is to increase dietary intake of unrefined fatty acids and or supplement the diet with unrefined fatty acids.
- Check for concurrent fungal infection. Remedy with a higher dose of Salvestrols if present.
- Check elimination of cellular debris from cancer cell death.
- Check stress levels. Remedy this with daily yoga, meditation and/or other relaxation techniques.
- Don't let the patient succumb to discouragement. Remedy this by letting the patient know that the disease took many, many years to develop and may take many, many months to resolve.

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