VALTYRON

CBC GROUP

A REVOLUTIONARY NEW APPROACH TO BLOOD PRESSURE CONTROL-AS NATURE INTENDED

Cardiovascular disease-an unmet growing challenge

Cardiovascular disease is one of the leading causes of death world-wide. According to the latest statistics from the World Health Organisation (WHO) around 20 million people die from heart disease globally every year. Hypertension is one of the major controllable risk factors associated with cardiovascular disease events such as myocardial infarction, heart failure and end-stage diabetes. Various synthetic pharmaceuticals are widely used to treat cardiovascular disorders and in the USA alone, current annual antihypertensive costs approximately $15 billion. WHO estimates that by 2020, heart disease and stroke will have surpassed infectious diseases to become the leading cause of death and disability worldwide.

Causes unknown but hypertension is a major factor

The causes of cardiovascular disease are diverse, but atherosclerosis(thickening of the artery wall as a result of accumulation of fatty deposits of cholesterol) or hypertension(high blood pressure) are the most common. It is estimated that around a third of all cardiovascular disease deaths are due to coronary artery disease. Elevated blood pressure(BP) is well recognised as one of the major independent risk factors for cardiovascular disease. BP is controlled by a number of different interacting biochemical pathways and can be increased or decreased depending on which pathway predominates at any given time.

Valtyron-a new supplement to help maintain a healthy cardiovascular system

The heart is about the size of a person's fist and weighs between 200-425 g. During a person's life, a heart could have beaten more than 3.5 billion times. In a full day, the average heart beats 100,000 times, pumping about 2000 gallons of blood, but its' health is taken for granted until something goes wrong. Hypertension is one of the main causes of cardiovascular disease, until now few nutritional supplements have focussed on this condition or found to be effective. Valtyron provides, a new natural, safe and effective solution to blood pressure control.

Proven efficacy in hypertension

Valtyron is a natural peptide extract derived from sardine muscle, which has been extensively evaluated in scientific studies and proven to be safe, bioavailable and clinically effective in lowering blood pressure through a well understood mechanism of action.

A FOSHU Brand Leader in Japan now with EU Novel Food status

In Japan, Valtyron is one of the leading FOSHU (Foods for Specified Health Uses) ingredients commonly incorporated into supplements, health drinks, vegetable juices, and beverages such as teas. However unlike many FOSHU ingredients Valtyron has received recognition as a novel food in EU.

A patented, versatile natural ingredient with a world of potential

Valtyron is water soluble and heat stable, with no bitter taste, making it ideal for incorporation into a wide variety of presentations such as cereals or drinks as well as nutritional supplements. It is the subject of 23 patents and over 25 scientific publications reviewing its proven benefit in managing hypertension, one of the biggest health concerns in the world today.

CBC GROUP

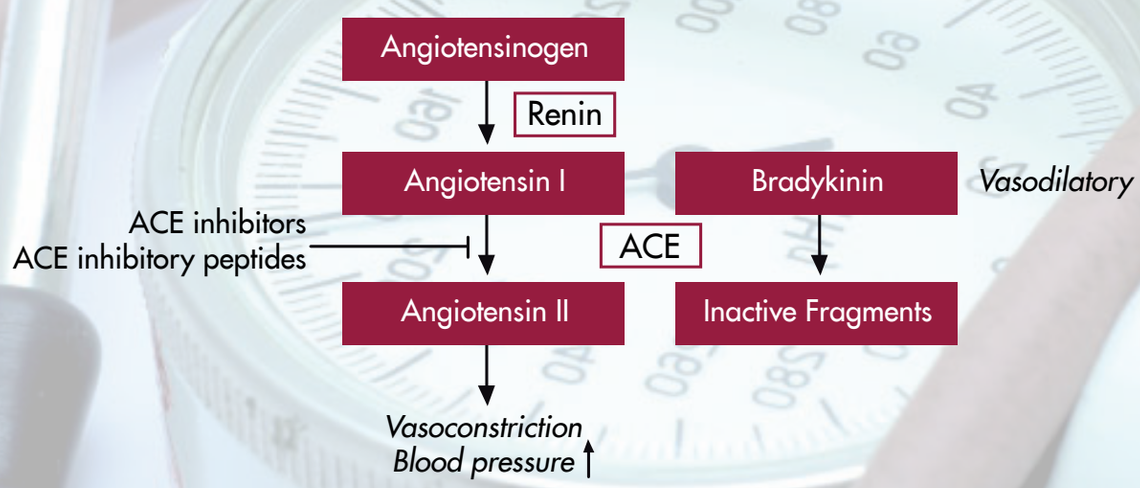
CBC (EUROPE) SRL, via E. Majorana, 2 - 20834 Nova Milanese (MB)
Tel: +39 0362.365079 Fax: +39 0362.41273
www.cbceurope.it chemical@cbceurope.it

VALTYRON

CBC GROUP

The Renin-Angiotensin pathway-and its role in blood pressure control

One of the key blood pressure control systems is the renin angiotensin system, which plays an important role in regulating arterial pressure. Renin converts angiotensinogen from the liver to angiotensin I, which in turn undergoes proteolytic cleavage to the biologically active angiotensin II. The latter step is carried out by angiotensin converting enzyme (ACE) which is highly expressed in vascular endothelium, particularly in the lungs. It converts the biologically inactive angiotensin I to the potent vasoconstrictor and cardiovascular trophic factor angiotensin II. Angiotensin II has many important actions, including increasing arterial pressure, increasing sodium and fluid retention, enhancing sympathetic adrenergic function and causing cardiac and vascular remodelling. Thus inhibition of this enzyme is seen as a key means to lower blood pressure and consequently the renin angiotensin system has become a key target for drugs combating hypertension.



ACE inhibition and natural compounds

The main problem with conventional ACE inhibiting, antihypertensive drugs is that they cause adverse effects. So safe and natural alternatives are desirable and some natural peptides have been identified which act on the renin-angiotensin system and also have the ability to reduce blood pressure.

The earliest reports of natural ACE inhibitors displaying an antihypertensive effect in vivo originated from snake venom. Thereafter many other natural ACE inhibitory peptides were discovered, some of which are derived from food proteins, including animal and plant derived peptides. Natural ACE inhibitors have now been derived from milk, corn and fish protein sources.

Numerous preclinical and studies in hypertensive human volunteers have been performed to determine the antihypertensive effects of food derived ACE inhibitors. These in vivo studies have demonstrated that some certain specific ACE inhibitory peptides significantly reduce blood pressure, after oral administration. The important observation from these trials is that these natural peptides generally have little or no effect on blood pressure in normotensive subjects suggesting that they exert no acute hypotensive effect. Therefore natural ACE inhibitory peptides can be safely applied as initial treatment in mild hypertensive individuals or as a supplemental treatment. Another advantage is that these peptides have not been associated with the harmful side effects reported for synthetic ACE inhibitors, such as dry cough, skin rashes and angiodema.

VALTYRON

CBC GROUP

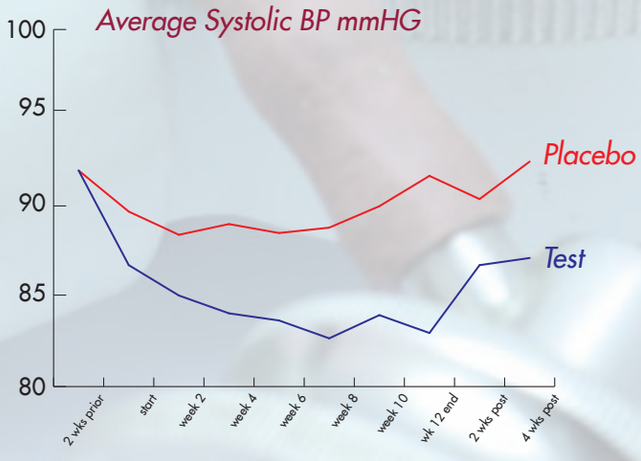
But not all natural ACE inhibitors are effective in-vivo antihypertensives

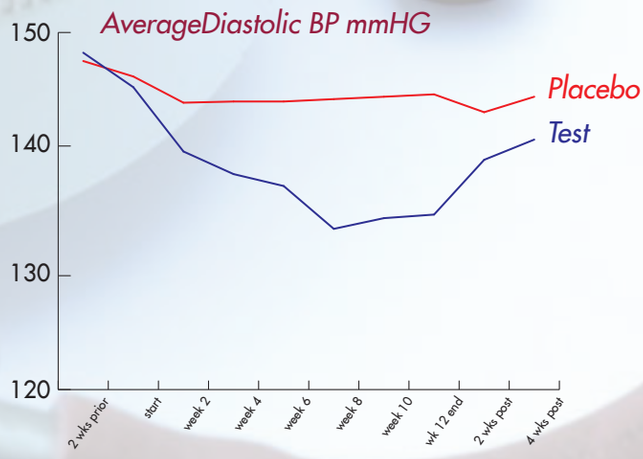
The potency of an ACE inhibitor is usually expressed as an IC 50 value, which is the inhibitor concentration leading to a 50% inhibition of ACE activity, in-vitro. However, due to an incomplete and often unknown bioavailability of the ACE inhibitory peptides following oral administration, it is difficult and unreliable to predict the in vivo antihypertensive effect, simply based on measures of inhibitory activity in vitro. In order to produce antihypertensive effects in vivo, the peptides have to be absorbed intact through the intestine and reach the cardiovascular system in an active form and in this regard, specific structural properties play an important role. However, if they are absorbed, in vivo comparative studies with the most clinically used ACE inhibitor-Captopril have shown that natural ACE inhibitory peptides deliver an antihypertensive effect with a higher activity than would be expected from their in vitro activity. The exact mechanisms underlying this observation have not yet been identified. However it is suggested that bioactive peptides may have a higher tissue affinity and are subject to slower elimination than captopril.

Valtyron-a natural, safe and effective ACE inhibitor

Around 25 scientific studies have been performed on Valtyron to establish safety and demonstrate bioavailability and establish efficacy in managing hypertension. Typical of the studies is a placebo controlled clinical investigation with matched patient controls, which identified that typically the systolic blood pressure of patients untreated with classical pharmaceutical interventions and classed as 'moderately hypertensive individuals' and who received Valtyron, saw their blood pressure reduced from 145 mmHg at the start of the trial to 134mm Hg after 8 weeks which was maintained for the 12 weeks of the trial . A significant difference in blood pressure began to be seen at 2 weeks after the start of ingestion between the test diet group and the placebo group, and two-way analysis of variance revealed principal effects between the two groups, indicating that systolic pressure after the start of ingestion differed significantly between the Vlatyron and placebo subjects.

Furthermore, whereas in the Valtyron treated group, systolic pressure was significantly reduced during the period from 2 weeks after the start of ingestion to the 12 weeks of completion, no significant change in systolic pressure was noted in the placebo group. Moreover, in the Valtyron group diastolic pressure was significantly reduced 8 weeks after the start of ingestion, whilst in the placebo group, no significant change in diastolic pressure was noted.





Ingestion of Valtyron resulted in no significant change in heart rate, body weight, body mass index or haematological parameters and no abnormalities in subjective symptoms or findings from doctor's examination. No adverse events (dry cough, allergic reaction, itching sensation, gastrointestinal symptoms, etc.) were noted.

The results from this study together with those from other similar published trials demonstrate that Valtyron is highly safe and exerts modest effects in lowering systolic and diastolic pressure in untreated individuals with high/ normal blood pressure and untreated individuals with hypertension.

VALTYRON

CBC GROUP

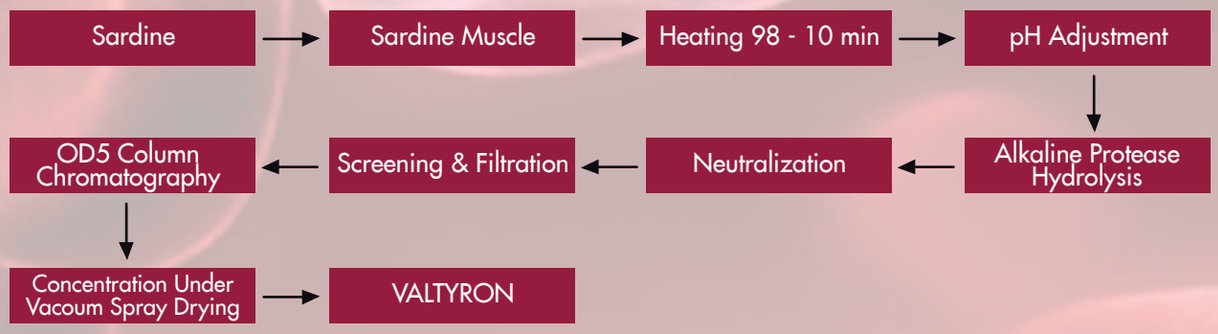
A REVOLUTIONARY NEW APPROACH TO BLOOD PRESSURE CONTROL-AS NATURE INTENDED

About Valtyron

Valtyron is a natural peptide derived from hydrolysed sardine fish meat containing the bioavailable dipeptide, Val-Tyr, which has been demonstrated to act as an antihypertensive in humans.

Only 100% sardine fish meat is used in the preparation of Valtyron which means that in comparison to other Marine sources such as Bonito, it is derived from a highly sustainable natural raw material.

Valtyron® Manufacturing Process



Valtyron® Regulatory Status

USA	Food Use	Authorized as a FDA Notified GRAS substance - GRN000360; FDA, 2011
EU	Food Use	Approved as a Novel Food - OJ L031/0048:0046, 2011

Features & Advantages

Featured of VALTYRON®

- Sardine peptide derived from sardine muscle hydrolyzate
  - A cluster of 2-3amino acids
- Raw Material
  - 100 % sardine
- Patent
  - International patents are as follows
  - NOVEL PEPTINE Y-2
  - NOVEL PEPTINE SY

  In addition, obtained 25 national and international patents

Advantages of VALTYRON®

- Comparison with competitors products

	Val-Tyr content	ACE Inhibitory value (IC50)	Observed in human plasma	Use Level
VALTYRON	175,8 mg/100g	52,4 µg/ml.	O	0,6 g/serving
Thermolysin digest of dried bonito	27,2 mg/100g	50,2 µg/ml.	X	1,5 g/serving

CBC GROUP

CBC (EUROPE) SRL, via E. Majorana, 2 - 20834 Nova Milanese (MB)
Tel: +39 0362.365079 Fax: +39 0362.41273
www.cbceurope.it chemical@cbceurope.it