

6 U 4 P 0

VOUR

HEART



November 2018

HEALTH · NUTRITION · MATERIALS

Executive summary

Cardiovascular disease (CVD) is the leading cause of mortality worldwide, accounting for 17.7 million deaths each year.¹ Understanding the potential causes of heart conditions is key in lowering this number and, with more information available at people's fingertips than ever before, a **prevention-led** approach may be the solution to improve the health of populations worldwide. The key to a healthy heart is supporting the three pillars of cardiovascular health: cholesterol and triglycerides levels, blood pressure and **blood flow**.

Adequate nutrition is vital in supporting heart health. A balanced diet of healthy foods and reaching the recommended daily intake of all essential vitamins and minerals is highly recommended to support the normal functioning of the body and help prevent the onset of disease. However, for many people, achieving the necessary levels of micronutrients through diet alone can be difficult. In these cases, supplementation provides a simple and convenient way for individuals to reach the desired intake. In fact, emerging research has shown certain bioactive compounds can help to address specific areas of heart health, with it being over a decade since scientists first found evidence that active components in tomatoes may have a natural **anti-thrombotic** effect and a role to play in maintaining healthy platelet aggregation.^{2,3} Advances such as these have paved the way for manufacturers to develop breakthrough natural ingredients, such as DSM's **Fruitflow®** – the world's first natural, scientifically supported solution for healthy blood flow, with an Article 13.5 health claim approved by the EU Commission on the basis of a positive EFSA opinion.⁴ Derived from tomato concentrate, Fruitflow[®] is a water-soluble, highly concentrated form of bioactives that contains over 30 known antiplatelet compounds and is suitable for use in food supplements.

This whitepaper examines the importance of healthy blood flow in overall cardiovascular health, before summarizing the growing body of scientific evidence to support the potential role of the dietary antiplatelet Fruitflow[®] in the **primary prevention of CVD**.

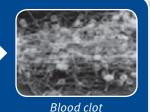
Healthy circulation for healthy hearts

The cardiovascular system supports a variety of functions in the human body, from regulating temperature and pH levels, to removing waste and transporting oxygen and nutrients to the brain and other organs. Previously often overlooked, healthy blood flow, or circulation, is of particular importance as it not only ensures the right amount of oxygen-rich blood is delivered around the body, but also reduces unnecessary strain on the heart. However, there are a range of risk factors that can result in poor blood circulation with the primary cause often being the clumping together of platelets in the blood. Platelets can play an important role in the body following injuries, clotting in an effort to prevent blood loss. Yet, if they become too 'sticky' then these activated platelets can aggregate inside blood vessels – making it harder for the blood to flow around the body and increasing the likelihood of unneeded, and potentially dangerous, blood clots. Additionally, activated platelets can also produce plaques which may then build up, resulting in the development of atherosclerosis – narrowing the arteries and restricting blood flow. Stress, obesity, pregnancy and both inactivity and extreme exercise all increase the likelihood of platelet aggregation.



Smooth platelets





Platelet aggregation involves a reversible **activation** phase followed by an irreversible **aggregation** stage



Recommendations for an effective prevention-led approach

Unfortunately for many, poor blood circulation is often not addressed by physicians until a significant build-up of risk is present. Activated platelets accelerate the issue, but the medical interventions that are currently available are not recommended for use in primary prevention for individuals who are not in immediate danger of developing further cardiovascular problems.

For those who have already experienced a cardiovascular event or when other CVD risks including high blood pressure have been identified, drugs with an antiplatelet effect, such as aspirin, are often recommended as secondary prevention for maintaining healthy blood circulation. However, aspirin has been linked to a range of negative health consequences. This includes stomach damage, allergic reactions and an increased likelihood of strokes. Indeed, a recent study revealed that daily aspirin intake may cause events of major bleeding.⁵ This negative side-effect has been well-publicized in the media, including the New York Times. Meanwhile, Fruitflow[®] on the other hand acts as a **natural blood thinner** and is **easy on the stomach**. With **no side effects**, Fruitflow[®] gets to work immediately and its benefits are long lasting, making it ideal for **primary prevention**.

A prevention-led approach to maintaining good cardiovascular health is now recommended by a variety of leading authorities, including the European Society of Cardiology (ESC). Indeed, in 2015 it launched the ESC Prevention of CVD Programme in an effort to promote effective secondary prevention.⁶ Regular exercise and a balanced diet are highly recommended for a healthy heart, including helping to contribute to healthy blood flow. However, changes in modern lifestyles mean this may not be achievable or convenient to many. The World Health Organization (WHO) suggests that as many as one in four adults globally do not get enough exercise, while a study by charity Diabetes UK suggests 66 percent of people in the UK eat three or fewer portions of fruit or vegetables a day.⁷⁸ Now recommended by over half of general practitioners and pharmacists, the use of supplements offers a reliable and effective method of improving an individual's overall wellbeing, without requiring a drastic lifestyle change.⁹

Additionally, the demand for products to support specific targeted health concerns is clear. Driven by consumers now understanding and placing more value on health than ever before, the global wellness market was worth approximately \$3.7 trillion in 2015 and continues to grow.¹⁰ As trends shift towards a more holistic, and preventative, approach, people are looking for ways to improve their health beyond essentiality. Prepared from tomato concentrate using patented processes, Fruitflow[®] is a **breakthrough natural dietary antiplatelet** for use in food supplements and a selected range of foods and beverages. With proven success, it gives people the opportunity to address concerns they have about their blood flow and can be easily integrated into their daily diet.



Fruitflow[®]: how it's made

The part of a tomato containing an antiplatelet is actually very small, with the bioactive compounds found only in the jelly around the tomato seeds. Fruitflow® is extracted from this jelly in sun-ripened tomatoes. The selected tomatoes are crushed to a paste, then the skin and seeds are removed. The bioactive compounds responsible are extracted from the clear juice and then highly concentrated to create Fruitflow®.

Fruitflow[®] has been evaluated by EFSA and was granted the first approved Article 13.5 (proprietary) health claim in 2009:

*"Fruitflow® helps maintain normal platelet aggregation, which contributes to healthy blood flow."*¹¹

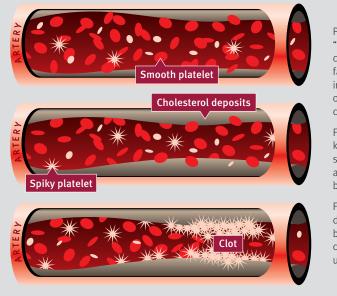
The science behind Fruitflow®

Fruitflow[®] was discovered in 1999 at the Rowett Research Institute by Professor Asim Duttaroy, and since then has been the subject of numerous clinical studies – with ten different human trials to date to support its **benefits for cardiovascular health**. These studies focused on a variety of different areas, from acute and chronic effects to the safety implications of over-consumption, to fully consider all aspects of safety and effectiveness, and found a 97% effectiveness in test subjects.

For instance, a seven-hour time course study was carried out in 23 cannulated human subjects to determine the efficacy of a supplement drink containing Fruitflow[®] and both the onset and duration of antiplatelet effects. The results found a significant inhibition of baseline platelet function three hours after consumption, which lasted for 12 hours.¹² This was later followed up by a double-blinded, placebo-controlled crossover study conducted on 90 healthy individuals with normal platelet function to determine the suitability of Fruitflow[®] as a dietary supplement. Again, **significant reductions in** *ex vivo* **platelet aggregation** were observed three hours after supplementation.¹³

When taken regularly (once a day), the maintenance of normal platelet aggregation is continuous and, unlike stronger medical interventions, the prolonged intake of Fruitflow[®] does not result in adverse side effects, allergic reactions or an increased risk of bleeding. Provided in a powder format, it is ideal for use as a daily supplement with a recommended dosage of **150mg**.

Mechanism of action



Platelets can become "spiky", i.e. more prone to clotting due to a variety of factors such as stress, inactivity and age (being over 40), diet and high cholesterol.

Fruitflow[®] works by keeping blood platelets smooth to avoid aggregation inside blood vessels.

Fruitflow[®] does not disrupt the rest of the blood clotting process, so clotting will take place as usual after injury.

Proven efficacy

2017 O'Kennedy et al. study

A recent randomized controlled trial compared Fruitflow[®] and aspirin. A total of 47 healthy subjects took part in a double-blind trial that examined the platelet responses to both Fruitflow[®] and aspirin. Acute and seven-day treatments with 75mg aspirin were compared with control (with and without concomitant Fruitflow[®]) over a five-hour time course. Platelet aggregation response agonist, platelet thromboxane A2 release, plasma clotting times and time to form a primary haemostatic clot were all measured as a comparison.

The results highlighted that the platelet suppression observed after consuming Fruitflow[®] is approximately one-third of the suppression following daily aspirin consumption, with no side effects. The reversible action of Fruitflow[®] means it is less likely to overextend over time to form a clot than aspirin, making it more suitable – and safer – for use in primary prevention.¹⁴

Securing safety

Compounds found in Fruitflow[®] have been shown to affect many aspects of platelet function, including thrombin generation. Therefore, in the trials, it was vital to understand whether any effect on the intrinsic or extrinsic clotting pathways could be detected, alongside antiplatelet effects. In all studies undertaken, clotting time measurements showed no significant increases from baseline levels.¹⁵

Fruitflow[®] for blood pressure

In addition to promoting good blood flow, there is initial scientific evidence to support the role of Fruitflow[®] in wider heart health. A study from the University of Oslo has shown Fruitflow[®] to have a positive effect on blood pressure, another important pillar of good cardiovascular function. The randomized, placebo controlled, double blind cross-over study involved twelve males that had been identified as being at risk of developing hypertension. All subjects refrained from using any dietary supplements for at least one month before the study to ensure the validity of results. The study compared two interventions with the supplement, separated by at least seven days. The results found a single dose of 150mg Fruitflow[®] resulted in a **significant reduction in 24-hour average blood pressure**.¹⁶ Additionally, the study also showed a reduction in platelet aggregation, echoing the findings of previous research and further supporting the beneficial effects of Fruitflow[®] for cardiovascular health.

Hyperactive platelets, a cause of platelet aggregation, can also lead to the development of atherosclerosis – which can, in turn, cause myocardial infarctions and cerebrovascular haemorrhages if the atherosclerotic plaques rupture. The results of this study show that dietary antiplatelets, such as Fruitflow[®], can have a **positive impact on wider cardiovascular health** to improve the lives of many across the world.



Success story: Fruitflow[®] in action

While available as an ingredient, Fruitflow[®] is also commercially available in the UK as a branded product, Fruitflow[®]+ omega 3 and has been wellreceived by consumers and healthcare professionals since its launch.

Expert opinion from Dr Ann Robinson, GP:

"We are looking for products that are a safer alternative to aspirin. So when we're talking about primary prevention, the idea that there could be a dietary product that really resonates with people as being natural and less prone to side effects, and the fact that [these products] could have such good efficacy is really attractive."

Positive feedback from satisfied consumers:

"The world needs to hear about this – it works."

"It transformed my cold feet, pins and needles almost immediately."

"Natural product, proven to improve circulation, with none of the sideeffects seen with aspirin – what's not to like?"

"I would also recommend it to anyone who is worried about strokes or DVTs."

Do more with nutrition

According to the European Society of Cardiology, cardiovascular disease costs EU economies as much as €210 billion a year – with almost 49 million people living with the condition across the region.¹⁷ To reduce pressure on healthcare services and the costs associated with treating cardiovascular incidents, maintaining a healthy heart is key. A healthy diet and regular exercise should be adhered to for optimal cardiovascular health, supported by nutritional interventions such as supplements where appropriate.

Co-innovation with DSM

As a science-based company, DSM's customers benefit from its unparalleled scientific and application expertise alongside its extensive portfolio of nutritional ingredients. DSM is dedicated to working in partnership with customers to support innovation and offers access to consumer insights, prototype development and brand activation strategies, as well as cobranding opportunities.



Quality for Life For DSM, quality is a way of life. This is the core of Quality for Life[™]. Quality for Life[™] is the mark of quality, reliability and traceability. It means that DSM customers are getting the best ingredients, knowing the source on which they depend. Quality for Life[™] means sustainability. It symbolizes our commitment to our environment, consumers, our business partners, our people and the regulatory framework that governs our operations. With the Quality for Life[™] seal, we aim to ensure peace of mind for your and for your customers.

Do you want to differentiate your cardiovascular health brand with a proven and natural solution for efficacious CVD prevention? For more information or a free consultation, please contact: *Marketing.DNPE@dsm.com*

References

- World Health Organization, 'Cardiovascular diseases (CVDs) fact sheet', http://www.who.int/mediacentre/factsheets/ fs317/en/ Accessed on: 17th October 2017.
- J. Yamamoto et al., 'Tomatoes have natural anti-thrombotic effects', British Journal of Nutrition, vol. 90, 2003, p. 1031-1038.
- K. Asim et al., 'Effects of tomato extract on human platelet aggregation in vitro', Platelets, vol. 12, 2001, p. 218-227.
- European Food Safety Authority (EFSA), 'Water-soluble tomato concentrate (WSTC I and II) and platelet aggregation', *The ESFA Journal*, vol. 7 issue 5, 2009.
- The ASCEND Study Collaborative Group, Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus, The New England Journal of Medicine. Available at: https://www. nejm.org/doi/full/10.1056/NEJM0a1804988.
- European Society of Cardiology', 'ESC prevention of CVD programme – about the programme'. https://www.escardio. org/Education/ESC-Prevention-of-CVD-Programme/Furtherreading-&-educational-material/about-the-programme Accessed on: 27 April.
- World Health Organization, 'Physical activity fact sheet', 2017, http://www.who.int/mediacentre/factsheets/fs385/en/ Accessed on: 23 November.
- Diabetes UK, 'Brits failing to meet the recommended daily allowance of fruit and veg', 2017, https://www.diabetes.org. uk/about_us/news/brits-failing-to-meet-the-recommendeddaily-allowance-of-fruit-and-veg Accessed on: 27 April.
- 9. DSM, 'Perception of nutritional supplements', 2017.
- Global Wellness Institute, 'Global wellness economy monitor – January 2017', 2017.
- 11. Op. cit. (European Food Safety).
- N. O'Kennedy, 'Effects of antiplatelet components of tomato extract on platelet function in vitro and ex vivo: a time-course cannulation study in healthy humans', *Am J Clin Nutr*, vol. 84, 2006, p. 570-579.
- N. O'Kennedy, 'Effects of tomato extract on platelet function: a double-blinded crossover study in healthy humans', *Am J Clin Nutr*, vol. 84, 2006, p. 561-569.
- N. O'Kennedy, 'A randomised controlled trial comparing a dietary antiplatelet, the water-soluble tomato extra Fruitflow, with 75mg aspirin in healthy subjects', *European Journal of Clinical Nutrition*, vol. 71, 2017, p. 723-730.
- N.O'Kennedy et al., 'Fruitflow[®] the first European Food Safety Authority-approved natural cardio-protective functional ingredient', *European Journal of Clinical Nutrition*, vol. 51, 2017, p. 461-482.
- N. O'Kennedy et al., 'Consumption of Fruitflow[®] lowers blood pressure in pre-hypertensive males: a randomised, placebo controlled, double blind, cross-over study', *International Journal of Food Sciences and Nutrition*, vol. 69, issue 4, 2018, p. 494-502.
- European Society of Cardiology, 'About Cardiovascular Disease in Europe 2017 Statistics', 2017, https://www. escardio.org/The-ESC/Press-Office/Fact-sheets.

Although DSM has used diligent care to ensure that the information provided herein is accurate and up to date, DSM makes no representation or warranty of the accuracy, reliability, or completeness of the information. This white paper only contains scientific and technical information on the role of Fruitflow® for healthy blood flow. Country or region-specific information should also be considered when labeling or advertising to final consumers. This white paper does not constitute or provide scientific or medical advice, diagnosis, or treatment and is distributed without warranty of any kind, either expressly or implied. In no event shall DSM be liable for any damages arising from the reader's reliance upon, or use of, these materials. The reader shall be solely responsible for any interpretation or use of the material contained herein. The content of this document is subject to change without further notice. Please contact your local DSM representative for more details. All trademarks listed in this white paper are either registered trademarks, trademarks or licensed trademarks of DSM group of companies in the Netherlands and/or other countries, unless explicitly stated otherwise.

© DSM Nutritional Products 2018