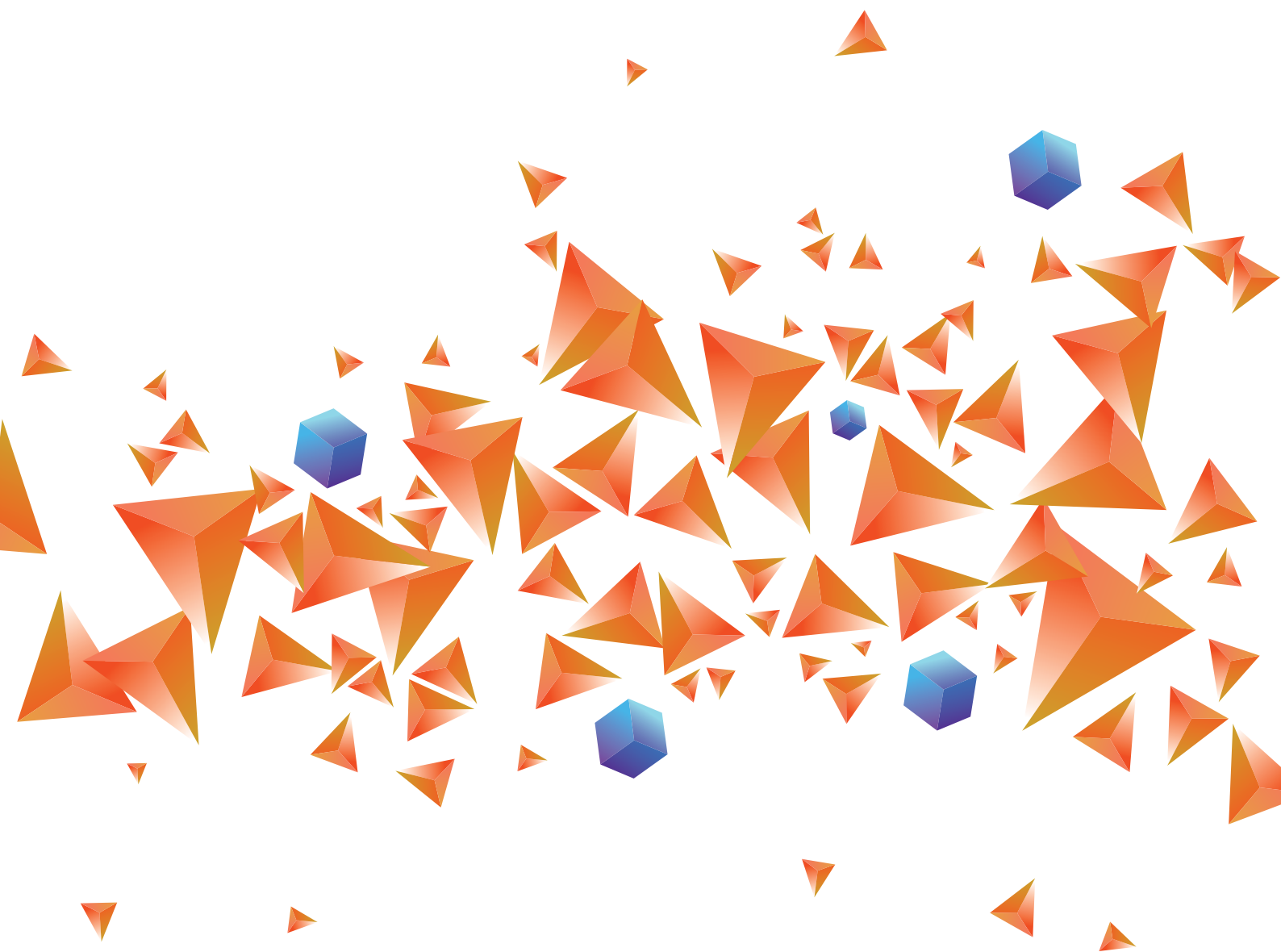




NEW MARKET OPPORTUNITIES WITH **CURCUMIN C3 REDUCT®**



EXECUTIVE SUMMARY



Sabinsa has developed C3 Reduct®, a curcuminoids-based ingredient that has been scientifically shown to boost organ health and deliver a range of other targeted functionalities. This makes it ideal to help manufacturers meet consumer health and wellness expectations – and tap new opportunities in growing markets such as sports nutrition. C3 Reduct® is the only reductive metabolites of curcuminoids on the market to have been approved as a Novel Food by the European Food Safety Authority (EFSA).

Consumers are increasingly aware that impaired organ health, high stress levels and immune system problems are issues that can significantly impact their quality of life. Since the Covid19 pandemic, they are increasingly looking for natural, functional preventive solutions that can support their efforts to keep fit and healthy.

There is huge scope for product innovation here. The global antioxidants market was valued at USD 3.4 billion in 2020 and is projected by some market researchers to reach USD 7.4 billion by 2031. The global sports nutrition market size meanwhile was valued at USD 34.8 billion in 2020 and is projected to reach USD 67.9 billion by 2030.¹

C3 Reduct® can help manufacturers to capitalise on these trends by offering functionalities that no other curcumin-based product can deliver. Curcumin, the principal curcuminoid sourced from the spice turmeric, has gained increasing consumer recognition for its multiple health benefits, in particular its antioxidant and anti-inflammatory properties. C3 Reduct® has been shown to deliver even more outstanding antioxidant and anti-inflammatory properties than the parent curcuminoids.

The key reason for this is that in C3 Reduct®, curcumin is converted to tetrahydrocurcumin (THC). This means that it is directly and easily assimilated in the body as an active metabolite. This is important, as THC has far better bioavailability than curcumin.

From a consumer point of view therefore, C3 Reduct® is an EFSA-approved product that delivers functionality, without the need for high dosages or added ingredients. The product also has self-affirmed GRAS (generally regarded as safe) status in the US.

The purpose of this White Paper is to help manufacturers understand the functional benefits of C3 Reduct®, and identify market opportunities in bringing cutting edge health, wellness and sports nutrition products to consumers.

1. <https://www.alliedmarketresearch.com/sports-nutrition-market>

THE WONDER OF CURCUMIN

- European imports of turmeric increased by over 69 % in terms of volume and by over 73 % in terms of value between 2015 and 2019.² Key drivers include an ageing population looking for products to support longevity, and the growing number of health-conscious consumers are concerned about issues such as organ health that declines with age.
- Curcumin, a natural compound present in the spice turmeric, has been the focus of clinical investigations for centuries. Ancient Ayurvedic texts wrote about the health benefits of turmeric almost 2500 years ago, identifying its usefulness in treating rheumatism, asthma, liver disorders and various allergies³.
- Recent studies have shown that curcumin can improve systemic markers of oxidative stress⁴ – a catalyst for vital organ complications.⁵ Today, turmeric is extensively used in Indian cuisine, as well as a preservative, colouring agent and flavouring in drinks. Curcumin is often available in several forms including capsules, tablets, ointments, energy drinks, soaps, and cosmetics.⁶



WHAT MAKES C3 Reduct® different?

- Sabinsa's C3 Reduct® is an important new milestone in fully exploiting the health benefits of curcumin. The pharmacological activities of C3 Reduct® – delivered directly to the body – provide possibilities for use as a natural antioxidant and anti-inflammatory across a wide range of products, from organ and oral care to sports performance products.

— What are THC's?



Tetrahydrocurcuminoids (THCs) are a colourless or white metabolites of curcuminoids, usually formed in the body. They have the key advantage of having higher bioavailability and physiological stability than – while retaining all the beneficial properties of – parent curcuminoids.



The knowledge that gut resident bacteria metabolise curcuminoids to THCs – a highly powerful and stable reductive metabolite, conferring similar yet stronger benefits than the parent curcuminoids – inspired Sabinsa to explore reductive metabolites in greater depth. The objective was to develop a product that delivers more functionality at lower doses than other conventional curcumin-based products on the market.

95%



C3 Reduct® has been designed to fully harness the benefits of THCs. The product is the hydrogenated derivative of the curcuminoids from Curcumin C3 Complex® and contains a minimum of 95 % THCs.

Critically, C3 Reduct® is more readily absorbed through the gastrointestinal tract than curcumin and can be thus directly assimilated more efficiently.

2. <https://www.cbi.eu/market-information/natural-ingredients-health-products/turmeric/market-potential>

3. Priyadarsini K.I. The chemistry of curcumin: From extraction to therapeutic agent. *Molecules*. 2014; 19:20091–20112. doi: 10.3390/molecules191220091.

4. Sahebkar A., Serbanc M.C., Ursoniuc S., Banach M. Effect of curcuminoids on oxidative stress: A systematic review and meta-analysis of randomized controlled trials. *J. Funct. Foods*. 2015;18:898–909. doi: 10.1016/j.jff.2015.01.005.

5. Pizzino G, Irrera N, Cucinotta M, Pallio G, Mannino F, Arcoraci V, Squadrito F, Altavilla D, Bitto A. Oxidative Stress: Harms and Benefits for Human Health. *Oxid Med Cell Longev*. 2017; 2017:8416763. doi: 10.1155/2017/8416763. Epub 2017 Jul 27. PMID: 28819546; PMCID: PMC5551541.

6. Gupta S.C., Patchva S., Aggarwal B.B. Therapeutic Roles of Curcumin: Lessons Learned from Clinical Trials. *AAPS J*. 2013; 15:195–218. doi: 10.1208/s12248-012-9432-8

KEY MARKET OPPORTUNITIES WITH C3 REDUCT®

— Healthy living and wellness through organ health



Since spring 2020, there has been growing consumer demand for health products in Europe, especially for immunity-boosting and organ-health supplements. This is expected to be a long-term trend. Unsurprisingly, the global coronavirus pandemic has been one of the main factors driving this trend, as consumers seek to improve their immune systems.

To meet consumer expectations for functional, natural clean-label products, nutraceutical companies need to increase the effectiveness of their ingredients and products.

C3 Reduct® can help manufacturers appeal to consumers looking for science-backed products with enhanced and targeted functionality. For example, fibrosis in various organs – such as in the lungs and the liver – can occur for a variety of reasons and is a common condition. While this can occur due to variety of reasons, inflammation is the key denominator for fibrosis development. A key issue is the fact that current pharmaceuticals have difficulty in treating this condition. This is where the effective, targeted antioxidant and anti-inflammatory properties of C3 Reduct® can help.



When it comes to lung health, in unpublished trials, C3 Reduct® has been shown to significantly reduce the expression of inflammatory markers such as IL-6 and IFN γ in lung tissues of rats with bleomycin-induced pulmonary fibrosis. For liver health, C3 Reduct® has been shown to be effective in reducing inflammatory cell infiltration into the liver, which could enable developers to better target the market for liver health product.⁷

Consumers are increasingly knowledgeable and aware of the influence of gut health on various organs and are looking for products that support gut health in a preventive manner. C3 Reduct® has been shown to attenuate inflammatory responses and maintain colon health, by selectively inhibiting the enzymes of certain inflammatory pathways.⁸

— C3 Reduct® – and healthy ageing



Europe's ageing population is also driving demand for targeted products that support longevity, organ health and general wellbeing. Ageing is associated with degenerative muscular and skeletal conditions and neurological conditions such as Alzheimer's.



Better awareness among seniors of the benefit of taking preventative measures – and the will to live independently for longer – is creating new opportunities for functional products that support healthy ageing. Indeed, the growing importance attached to this issue is underlined by the fact that the United Nations declared this decade to be the Decade of Healthy Ageing.⁹



Nutraceutical products that help consumers to maintain brain health is a category that is only set to grow, and C3 Reduct® possesses excellent antioxidant and anti-inflammatory properties. In trials, THC, the major ingredient in C3 Reduct®, has been shown to reduce inflammation and thus neurodegeneration, because it possesses anti-amyloid activity. THC has also been shown to help reduce glutathione in the brains of diabetic rats, suggesting efficacy in protecting against lipid peroxidation-induced membrane damage.¹⁰



Another key issue with regards to healthy ageing is joint health, and the anti-inflammatory properties of C3 Reduct® hold significant promise in this field. Osteoarthritis (OA) is a chronic joint condition, affecting over 250 million people worldwide¹¹. Ongoing studies and existing literature beckon a promising role for the anti-arthritic effects of THC in OA and rheumatoid arthritis (RA). In particular, THC – but not curcumin – was shown to prevent glucose intolerance, which might be involved in exacerbating osteoarthritis.¹²

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10. Aynun N. et. al. 2008. Curcumin Structure-Function, Bioavailability, and Efficacy in Models of Neuroinflammation and Alzheimer's Disease. *The Journal of pharmacology and Experimental Therapeutics*. 326:196-208

11. Hunter D.J., Schofield D., Callander E. The individual and socioeconomic impact of osteoarthritis. *Lancet Nat. Rev. Rheumatol*. 2014; 10:437-441. doi: 10.1038/nrrheum.2014.44.

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— C3 Reduct® and sports nutrition

The market for sports nutrition products has grown steadily over the past decade and is projected to continue to expand. Health-conscious consumers are looking for products that boost performance and increase recovery speeds during and after sports activities – the most commonly used products tend to be protein powders and sports drinks.

Exertion during sport or physical activity can lead to inflammation in the body. Chronic inflammatory reactions can cause tissue injuries, leading to various disorders. The anti-inflammatory properties of C3 Reduct® hold significant promise in the development of effective sports nutrition products.

In addition to its anti-inflammation properties, THC has demonstrated significant functionality in maintaining energy balance within the body. Central to this is AMP-activated protein kinase (AMPK). AMPK is a central regulator of energy homeostasis, which coordinates metabolic pathways and thus balances nutrient supply with energy demand.

AMPK is important because it balances nutrient supply with energy demand and stimulates ATP-production under energy depleted conditions. C3 Reduct® has been shown to activate AMPK and help reduce excess glucose and fats by burning them for energy. Furthermore, C3 Reduct® has been shown to be more potent than curcumin in activating cellular energy balance.¹³

The colourless nature of THC also opens new opportunities in sports nutrition. Many products in this category are whey-based protein formulations that tend not to include curcumin, despite the proven functional benefits. Manufacturers are concerned that the yellow and potential off-notes will put consumers off. This has historically been a major hurdle in including curcumin in sports formulations.

C3 Reduct® overcomes these consumer perceptions precisely because it is colourless and flavourless. In addition, many sports nutrition manufacturers are small businesses that want to produce batches quickly. C3 Reduct® enables them to do so, without the need to halt production to clean equipment due to staining.



13. Teayoun K., Curcumin activates AMPK and suppresses gluconeogenic gene expression in hepatoma cells Biochemical and Biophysical Research Communications 388 (2009) 377–382

— C3 Reduct® for Oral Health

Oral diseases are widely prevalent around the globe. The global oral care market size was valued at USD 33.7 billion in 2021 and is expected to expand at a compound annual growth rate (CAGR) of 6.4 % from 2022 to 2030.¹⁴ The Global Burden of Disease Study 2019¹⁵ estimated that oral diseases affect almost 3.5 billion people worldwide, with oral cancer being one of the ten most common cancers in the world.

A recent clinical study was conducted on 31 canker sore and 29 gingivitis patients for 21 days.¹⁶ Patients were instructed to consume one chewable tablet of C3 Reduct®, containing 100 mg of THC_s, twice a day. Clinical symptoms improved within 14 and 21 days of treatment, with a significant reduction in reddening, burning sensation, and throat numbness in canker sore patients. In gingivitis patients, gingival appearance, bleeding and inflammation were shown to be significantly reduced through C3 Reduct® treatment.

— C3 Reduct® and diabetes

Diabetes is the fastest growing metabolic disorder in the world and a major cause of morbidity. In 2019, diabetes and kidney disease due to diabetes caused an estimated 2 million deaths.¹⁷ C3 Reduct® can help manage healthy sugar levels and should therefore appeal to consumers who are increasingly aware of the health risks attached to diabetes. Oral administration of C3 Reduct® showed a significant decrease in the level of blood glucose, with a significant increase in the level of plasma insulin in STZ-nicotinamide diabetic rats.¹⁸



C3 Reduct®

SOURCING AND SUPPLY CHAIN

- Ensuring sustainability along the supply chain is becoming an obligation for manufacturers, with consumers increasing demanding transparency about the journey of their product. As a major exporter of natural nutraceuticals, Sabinsa is strongly committed to building a sustainable and responsible supply chain that meets consumer expectations.
- In practice, this has meant adopting a contract farming model for medicinal plants over the past few decades, to create a network of farmers covering over 20 000 acres of India. Turmeric farmers are seen as partners, and the numbers joining the network increases every year. Farmers are assured mutually agreed prices and are trained in Good Agricultural Practices (GAP) and Good Field Collection Practices (GFCP) developed by the World Health Organisation.¹⁹
- Sabinsa is also working on reforestation programmes for growing selected species of medicinal plants, working alongside State Ministries, Forest Departments and farmer's groups.

14. <https://www.grandviewresearch.com/industry-analysis/oral-care-market>

15. <https://www.healthdata.org/gbd/2019>

16. Majeed M, Majeed S, Nagabhushanam K. 2020. Efficacy and safety of tetrahydrocurcuminoids for the treatment of canker sore and gingivitis. Evidence-Based Complementary and Alternative Medicine. 2020.

17. <https://www.who.int/news-room/fact-sheets/detail/diabetes>

18. Pari L, Murugan P. 2007. Antihyperlipidemic effect of curcumin and tetrahydrocurcumin in experimental type 2 diabetic rats. Renal Failure. 29(7): 881-889

19. <https://sabinsa.com/newsroom/media-coverage/2022/NuFFoods-Spectrum-Dr-Majeed.pdf>

COLOUR BENEFITS OF **C3 REDUCT®**

- While there is a great deal of scientific support when it comes to the functional benefits of C3 Reduct®, the fact that THC_s are colourless brings additional practical and marketing benefits. Using C3 Reduct® means no staining, either during processing or in the final consumer product. If a manufacturer wishes to change the colour of the product with a natural ingredient, this will not alter the product's functionality, nor its clean label properties. This means products using C3 Reduct® can be easily universally accepted.

AUTHORISATIONS AND **APPROVALS**

- Sabinsa has obtained Novel Food approval from the European Food Safety Authority (EFSA) for C3 Reduct® – the only curcuminoid to be awarded EFSA Novel Food status (Regulation 2015/2283)²⁰. This means that product developers can use C3 Reduct® safe in the knowledge that it meets and surpasses the most stringent thresholds for safety. The THC_s from turmeric are well characterised, and compliant with European Regulations. The novel food is safe and devoid of allergic potential.
- This Novel Food is intended to be used as food supplement (as defined in Directive 2002/46/EC) at a maximum daily dose of 140 mg intended for the adult population and excluding children. The product is approved as per Implementing Regulation EC 2022/96 amending Implementing Regulation (EU) 2017/2470.²¹ As this White Paper has outlined, numerous trials and studies have supported the safety and efficacy of C3 Reduct®.



20. <https://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX%3A32015R2283>

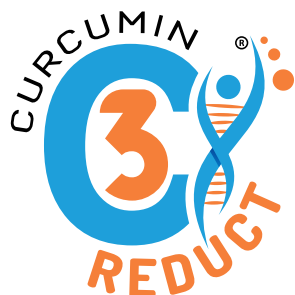
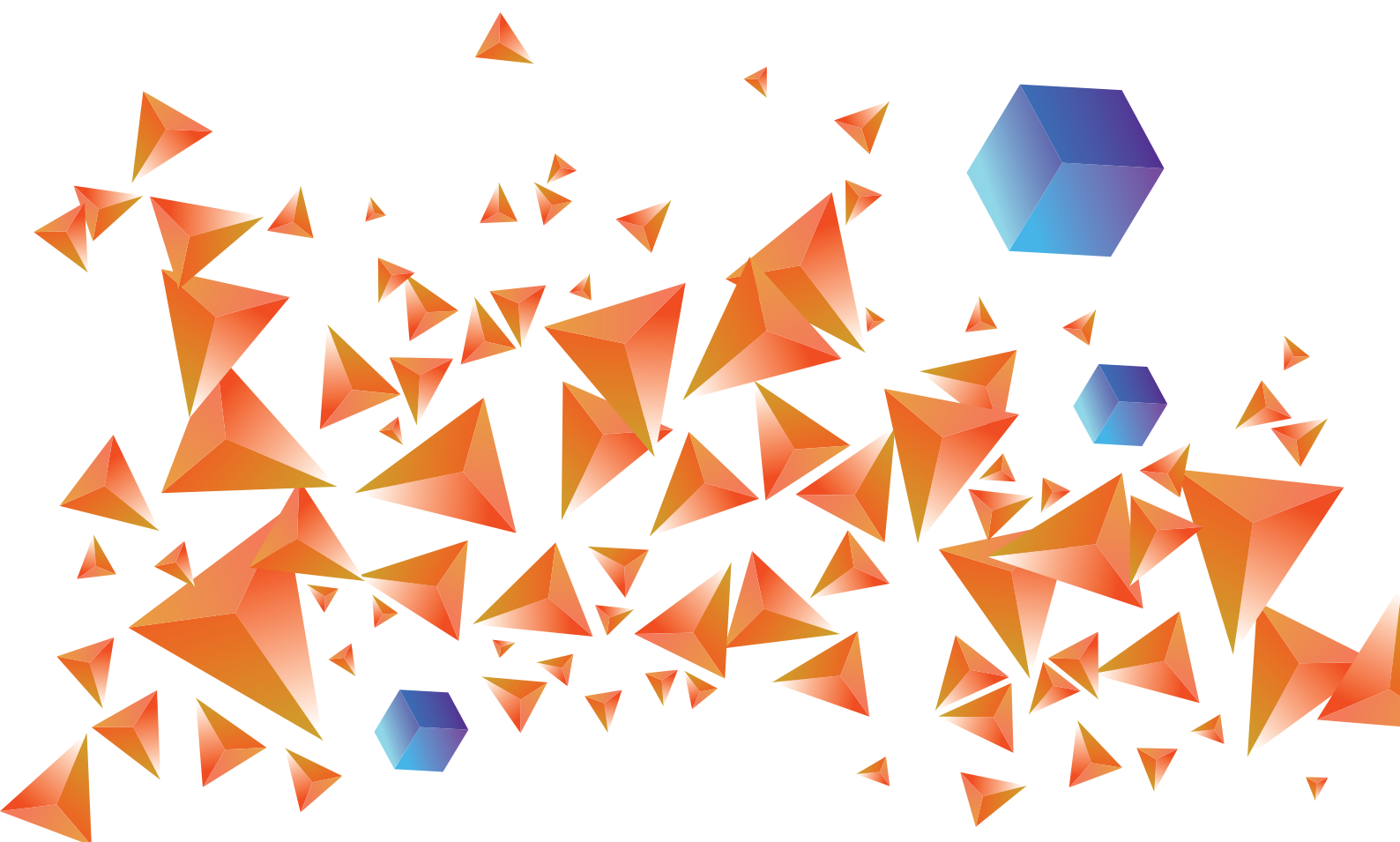
21. https://eur-lex.europa.eu/eli/reg_impl/2017/2470/oj

About **US**

Sabinsa Corporation, founded in 1988, is a manufacturer and supplier of herbal extracts, cosmeceuticals, minerals and specialty fine chemicals. Sabinsa's mission is to provide evidence-based natural products for human functional nutrition and well-being.

Its present operations have grown to employ 1 000 people worldwide in ten manufacturing, R&D and distribution facilities. Additionally, botanical cultivation efforts undertaken by the organisation now total nearly 40 000 acres to ensure sustainable supplies on its key products.

With more than 120 scientists working full time conducting ongoing research in Europe, India and the United States, Sabinsa continues to develop and patent beneficial nutrients for the world market.



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