



Advanced 4^{IN}1 Support

Multi-Target Natural Defence System with High Bioavailability



*The state-of-the-science, cost-effective,
immune support product that every adult
can't afford to be without.*

DISCLAIMER:

The information contained in this business-to-business (B2B) product information brochure is strictly for educational and informational purposes only. The efficacy of this food supplement has not been confirmed by European or other authorities. This brochure is intended exclusively for use with wholesaler and retail businesses, and not for business-to-consumer (B2C) sales support. The food supplement product is not intended to diagnose, treat, cure or prevent any infectious or other disease. All information presented here is not meant as a substitute for, or an alternative to, information from healthcare practitioners. Before using any food supplement, please consult your healthcare professional about potential interactions or other possible complications.

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Authorised health claims for Unidis Advanced 4:1 Support*

Vitamin C

- Vitamin C increases iron absorption and contributes to:
- maintaining the normal function of the immune system during and after intense physical exercise
- normal collagen formation for the normal function of blood vessels
- normal collagen formation for the normal function of bones
- normal collagen formation for the normal function of cartilage
- normal collagen formation for the normal function of gums
- normal collagen formation for the normal function of skin
- normal collagen formation for the normal function of teeth
- normal functioning of the nervous system
- normal energy-yielding metabolism
- normal functioning of the nervous system
- normal psychological function
- normal function of the immune system
- the protection of cells from oxidative stress
- the reduction of tiredness and fatigue
- the regeneration of the reduced form of vitamin E

Zinc

- Zinc has a role in the process of cell division, and contributes to:
- normal DNA synthesis
- normal acid-base metabolism
- normal carbohydrate metabolism
- normal cognitive function
- normal fertility and reproduction
- normal macronutrient metabolism
- normal metabolism of fatty acids
- normal metabolism of vitamin A
- normal protein synthesis
- the maintenance of normal bones
- the maintenance of normal hair
- the maintenance of normal nails
- the maintenance of normal skin
- the maintenance of normal testosterone levels in the blood
- the maintenance of normal vision
- the normal function of the immune system
- the protection of cells from oxidative stress

*Authorised according to EU Regulation No 1924/2006, as amended, the listed claims also having been incorporated into the Great Britain Nutrition and Health Claims Register (GB NHC Register).

No health claims have been authorised in the European Union for isoquercetin, quercetin, green tea or (-)-epigallocatechin gallate (EGCG). There are a number of non-authorised health claims for quercetin and green tea extract/flavonoids and these should not be used in conjunction with this product. For further information, please consult the [EU Register of Health Claims](#).

Beneficial effects of the ingredients at the dosages presented in the product, that have been substantiated in the scientific literature (see references cited in this educational brochure), are as follows:

Isoquercetin

- Immune system modulation
- Inhibits platelet aggregation
- Antiviral activity
- Antioxidant activity
- Anti-inflammatory activity
- Cardiovascular protective
- Enhanced psychostimulant response
- Cancer protective
- Mitochondrial biogenesis
- Capillary integrity
- Inhibits oxidation of fats

Zinc

- Immune system modulation
- Growth support
- Development support
- Repair support
- Metabolism support
- Inflammatory response support

Green tea EGCG

- Immune system modulation
- Cardiovascular disease protection
- Cancer protective
- Mitochondrial support

Vitamin C

- Immune system modulation
- Antioxidant activity
- Energy metabolism support
- Cofactor in numerous metabolic processes

Challenging times

The recent pandemic has made people much more conscious of the importance of self-care for their immune systems. Surveys of European populations conducted prior to 2020 showed highly variable patterns of supplement consumption in different countries. For example, a study of Italian students found 37% consumed food supplements (Montagnani *et al*, 2018), while another found only 10% of Lithuanian adults consumed them regularly (Dobrovolskij, 2018). Most commonly consumed ingredients are vitamins and minerals, often in multi-vitamin/mineral form. A 2014 study evaluating consumption of botanical ingredients in food supplements in 6 European countries (Finland, Germany, Italy, Romania, Spain and the United Kingdom) found that less than 20% of those screened consumed one or more botanical food supplement ingredients (Garcia-Alvarez *et al*, 2014).

A comprehensive survey of European consumers by Ipsos Public Health conducted on behalf of Food Supplements Europe in 2022 found that supplement use had dramatically increased compared with pre-pandemic patterns. Almost 90% of the carefully selected sample had taken food supplements in their lives, and 93% had done so in the past 12 months [Ipsos, 2022]. However, as shown from the top 10 supplements consumed (Fig. 1), these do not necessarily include those micronutrients with the strongest evidence of support for the immune system.

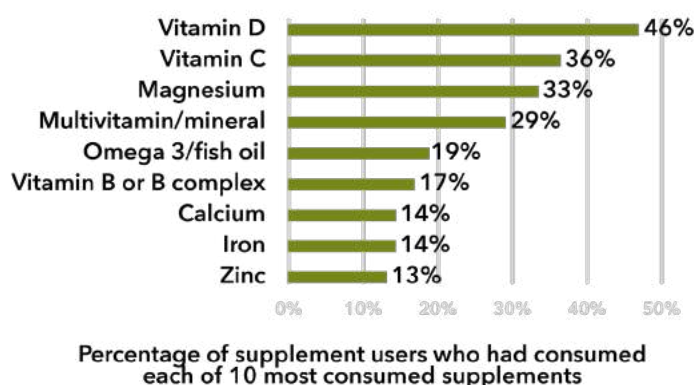


Figure 1. Top 10 food supplements taken in the past 12 months by European consumers (%). Data source: Ipsos (2022).

Unidis Advanced 4:1 Support synergy

The **Advanced 4:1 Support** formulation has been developed to provide the optimal combination and dosage of one mineral, one vitamin and two botanical sources to provide optimal immune support for adults. Many multi-nutrient products will contain some, or even most, of these 4 ingredients, but the forms and doses are rarely optimal. Conversely, those who select single source supplements, often fail to take the optimal combination or dosage to deliver the synergy offered uniquely by Unidis **Advanced 4:1 Support**.

The profound benefits of consuming all 4 ingredients and their respective dosages together, synergistically, is given below.

Isoquercetin – for super bioavailability



Isoquercetin is a flavonoid compound (secondary plant metabolite) that is found in a variety of fruits and vegetables, such as apples, onions, tea leaves, and berries. Along with other quercetin flavonols, it acts as an essential plant secondary metabolite, aiding germination, growth and the protection of plants from abiotic and biotic stresses.

Isoquercetin, along with its aglycone relative, quercetin (Fig. 1), has been studied extensively for its diverse roles in human health. This includes its antiviral, immune enhancing, antioxidant, anti-inflammatory, cardiovascular protective, psychostimulant and anti-carcinogenic activities, as well as their ability to inhibit lipid peroxidation (oxidation of fats), platelet aggregation and capillary permeability, and to stimulate mitochondrial biogenesis (Aguirre *et al*, 2011; Li *et al*, 2016; Kim *et al*, 2020; Mbikay & Chrétien, 2022).

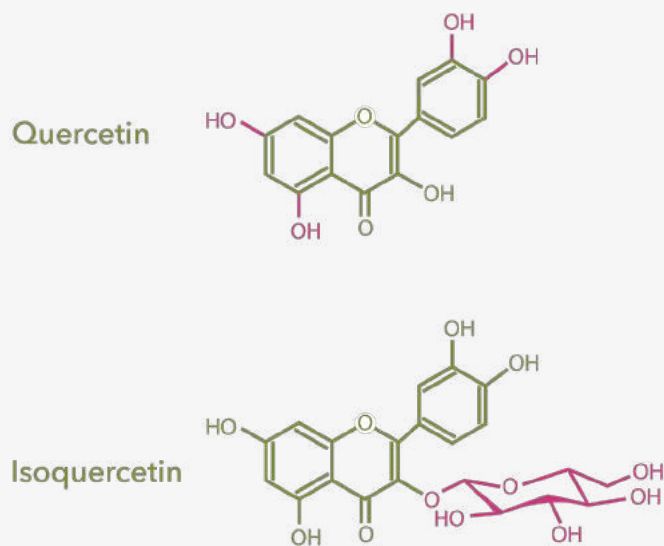


Figure 1. Structures of quercetin (= aglycone form) and isoquercetin (= glycosylated form).

While quercetin, being an aglycone (i.e. lacking an attached sugar molecule) has been found to show very favourable activity in in-vitro and ex-vivo studies, this has been less the case with human clinical studies (Mbikay & Chrétien, 2022). This limitation of quercetin is likely primarily linked to its poor bioavailability, in turn a function of its lipophilic (fat-loving) nature, so that relatively little crosses the gut epithelium and enters circulation (potentially as little as 2%) (Li *et al*, 2016).

Isoquercetin, the principle form found in onions, but not apples, can be regarded as “pro-quercetin” given it is metabolically converted to quercetin after entering the circulation. Its structure includes a single glucose molecule attached to position 3 of the carbon ring in the quercetin backbone, in place of the OH group. This makes it a glucoside, hence isoquercetin’s synonym, quercetin-3-glucoside. The addition of the sugar molecule in isoquercetin increases water solubility around 4-fold and dramatically improves transport across the intestinal lumen and allows rapid conversion to the highly bioactive quercetin form once absorbed (Mbikay & Chrétien, 2022).

Intakes of quercetin compounds vary greatly in different cultures, typically being in the range of 3-12 mg daily, but most is typically in the low bioavailability, aglycone form (Valentová *et al*, 2014). The biological activity of quercetin compounds is known to be potentiated by vitamin C (Nabavi *et al*, 2012).

Zinc – the immune essential



Of the top 10 most consumed ingredients found in the Ipsos (2022) survey, zinc, among the most important micronutrients for immune system modulation, was consumed by just 13% of those surveyed.

Zinc has multiple roles in the body, including its effect on normal growth, development, repair, metabolism, and maintenance of cell integrity as well as the function and modulation of the immune system, and in regulating inflammation (Bonaventura *et al*, 2015). Optimum serum levels for immune system modulation are significantly greater than those for growth and development (Iovino *et al*, 2018). Sub-optimal zinc intakes will become more common as more and more people transition from animal to plant-based protein sources, given fish, red meat, and poultry have traditionally been the most important sources of zinc. Additionally, only 15% to 50% of zinc in fortified foods and in food supplements may be absorbed, given it’s being complexed with phytate in the gut when consumed with phytate-rich foods (e.g. seeds, nuts, wholegrain cereals/grains, lentils, beans) (Roohani *et al*, 2013; Maares & Haase, 2020).

Green tea catechins – innate and adaptive immune maestro



The wide-ranging benefits of green tea consumption, ranging from general wellbeing and weight loss, through to reducing risk of cardiovascular disease and cancer, have been known for centuries (Fujiki *et al*, 2018; Shirakami & Shimizu, 2018). These benefits have long been related to the presence of a sub-group of flavonoid polyphenols called catechins, in particular the most abundant form, (-)-epigallocatechin gallate (EGCG). More recent research has shown that low and very high doses can mediate quite

different effects on the immune system, on mitochondria and through autophagy and many of the beneficial effects are related to the unique property of EGCG to bind to a specific laminin receptor (67LR) (Kim *et al*, 2014; see Figure 2).

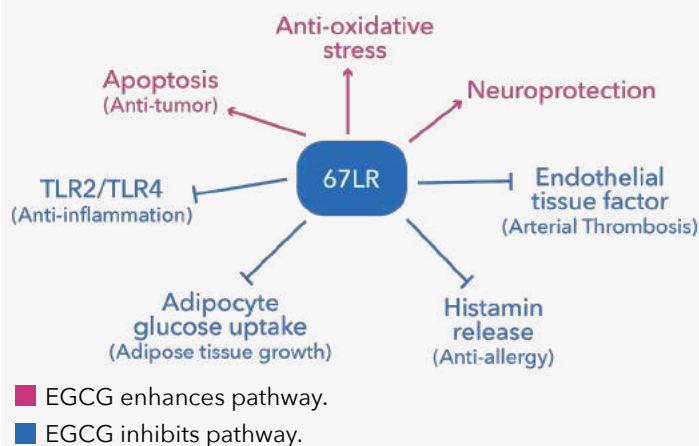


Figure 2. The multiple biological functions of EGCG mediated through the laminin receptor 67LR, specific to EGCG. Adapted from: Kim *et al*, 2014.

In 2018, a key molecular mechanism was discovered that might explain many of these effects. This relates to its ability to act as an immune checkpoint indicator that helps to block programmed cell death in crucial immune cells, namely T lymphocytes (Rawangkan *et al*, 2018).

Other research has confirmed EGCG's role in enhancing CD4+ T cell, and natural killer (NK) cell activity (Kim *et al*, 2016), as well as anti-inflammatory, antioxidant and antimicrobial activities (Singh *et al*, 2011; Reysgaert, 2018).

Green tea catechins' ability to modulate both the innate and adaptive sides of the immune system, makes it a key candidate in helping to prime the immune system in the face of infectious disease pressures (Chowdhury & Barooah, 2020).

Vitamin C



Vitamin C (ascorbic acid) is probably the most thoroughly researched micronutrient, with extensive data pointing to its activity as an antioxidant and an immune support agent (Carr & Maggini, 2017). However, its ability to act as a pro-oxidant, rather than an antioxidant, at high dosages (Pawlowska *et al*, 2019) and

its role as a cofactor, are often overlooked. Vitamin C has been found to be a vital cofactor that significantly enhances the effects of polyphenols (Nowak *et al*, 2018), such as the isoquercetin and EGCG in Unidis **Advanced 4:1 Support**.

Among other key functions is its role in recycling other antioxidants, facilitating iron absorption and aiding the conversion of cholesterol to bile acids, as well as being an essential cofactor in the synthesis of carnitine (Cahill & El-Sohehy, 2011).

Formulation and ingredients

Ingredients	Per 2 capsules	%NRV*
Japanese pagoda tree (<i>Styphnolobium [Sophora] japonica</i> L.) flower extract	102 mg	†
of which Isoquercetin	100 mg	†
Zinc (as citrate)	15 mg	150%
Green tea (<i>Camelia sinensis</i>) leaf extract	200 mg	†
of which EGCG	160 mg	†
Vitamin C (as L-ascorbic acid)	500 mg	625%
*NRV: EU Nutrient Reference Value. †NRV not yet established.		

Ingredients

L-Ascorbic Acid; Green Tea Extract (80% EGCG); Capsule shell: Hypromellose; Japanese Pagoda Tree Flower Extract (98% Isoquercetin); Zinc Citrate; Anti-caking agent: Magnesium Salts of Fatty Acids; Silicon Dioxide.

Directions for use

Adults and children above 12 years of age: Take 2 capsules per day, preferably with food (but not with cereals, bread or other phytate-rich foods), or as directed by your health professional.

Precautions, shelf life and storage

Not recommended during pregnancy and lactation without medical advice. Avoid use if you are known to have any allergies or hypersensitivities to any of the ingredients.

The shelf life of the product is 2 years from the date of manufacturing.

The product should be stored in a dry place at a temperature not exceeding 25°C. Protect from light. Keep out of reach and sight of children.

GMP manufacture in Europe

Unidis **Advanced 4-1 Support** is manufactured in Global Pharma CA SA Berezów 49A 26-130, Poland.

Global Pharma is a licensed and internationally accredited manufacturer of food supplements and operates to the highest standards of food safety and quality control. It is certified by the International Standards Organization (ISO) as a Safe Food Manufacturer (ISO 22000:2018) and relies on its Quality Management System (ISO 13485:2016). It complies with Good Manufacturing (GMP) and Good Hygiene Practice (GHP) in accordance with European Regulation (EC) No 853/2004 and, in Polish national law, the Act of 25 August 2006 on Food and Nutritional Safety (Journal of Laws of 2020, item 2021, as amended). The facility has implemented and maintains the Hazard Analysis and Critical Control Point (HACCP) system.



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