FRUIT JUICE
SCIENCE CENTRE

WHY WE SHOULD ALL LOVE OUR IMMUNE HEALTH INSIDE OUT

NEW RESEARCH SHOWS WHY GERMANS NEED TO GET IMMUNE FIT

FOREWORD:

PRIORITISE YOUR IMMUNE HEALTH:
THE ROLE OF FRUIT JUICE IN HEALTH AND IMMUNITY

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In the fight against Covid-19, our immune system is of vital importance.

More and more of us are on a mission to protect ourselves against the Covid pandemic. According to new research[1] commissioned by the Fruit Juice Science Centre – an evidence-backed health information body on fruit juice - 35% of Germans are more aware of the importance of the immune system. Added to this, Google Trends has revealed that searches for 'immune function' peaked in March 2020 - an impressive 700% rise from 2019.

Until Covid-19 came on the scene, we took our immune health for granted. Social distancing, face masks and thorough hand washing have all been implemented in a bid to reduce transmission of the illness, but optimising our immune response is also now a health must.[2]

Reassuringly, there are simple steps we can all take to help to strengthen our immunity and stay fighting fit all year round.

NUTRITION AND IMMUNE FITNESS: A MATCH MADE

Diet is one way of strengthening our immune system. Over recent years, blueberries, garlic, oranges, spinach and oily fish have been dubbed the immunity 'hero' foods, with fruit juice often being demonised. However, evidence shows that fruit juice - particularly 100% orange juice - has a host of health benefits and few, if any, of the supposed downsides.

In a nutshell, the high vitamin C content of orange juice is key for immune functionality. One 150 ml glass of 100% orange juice provides a staggering 84% of the Nutrient Reference Value (NRV – the minimum target for intake set by the EU) for vitamin C.

Vitamin C has also attracted significant interest in the context of the Covid-19 pandemic. The survey by the Fruit Juice Science Centre found that 31% of adults believe orange juice is best for immune health, with 21% identifying mixed fruit juice and 10% identifying pomegranate juice.

As well as vitamin C; folate, vitamin D, vitamin P (polyphenols) and omega-3 fatty acids have been proven to support our immune system.

Added to this, a healthy and diverse gut microbiota can be beneficial. Probiotics might be the obvious choice here, but prebiotics - compounds which feed beneficial micro-organisms in the gut - are also important. Plant-based foods and drinks, particularly fruits, vegetables and their juices, have prebiotic activity thanks to their rich content of fibre and plant polyphenols. Yet 57% of those surveyed weren't aware of the health-promoting polyphenols.

HEARD OF HESPERIDIN?

Add this word to your immune optimising dictionary as new emerging clinical evidence shows this type of polyphenol helps provide prebiotic goodness.

Found in citrus fruits and their juices, hesperidin has attracted the attention of scientists because it binds to the key proteins of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) – the virus that causes Covid-19 - meaning it could have anti-viral effects. Further research is planned to investigate these findings.[3] While vitamin C and folate are key players in fruit juice's immunity armoury, other bioactive compounds like hesperidin clearly play a part. Plus, polyphenols and vitamin C are both known to help in recovery by counteracting the cell-damaging effects of oxygen free radicals triggered by viral infections and the body's immune response to these.[4]

There's never been a better time to give a clear public message to the nation that consumption of 100% orange juice a day could play a pivotal role in helping get our immunity fit for purpose. With the Covid pandemic still with us, it's important that we all do more to get ready for the peak winter viral season. According to a study involving a sample of 1840 adults (778 adult men and 1062 adult women) sampled from the German National Nutrition Survey mean intake of fruit juice and nectar in Germany was 120g daily in 2012-2013.[5]

This report outlines the mounting health and wellbeing evidence behind fruit juice, as well as detailing how we can optimise and love our immune health inside out through an optimal diet.

HESPERIDIN HAS ATTRACTED THE ATTENTION OF SCIENTISTS BECAUSE IT BINDS TO THE KEY PROTEINS OF THE SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2)

JARGON BUSTER:

- **Antibody:** a protein component of the immune system that circulates in the blood. It recognises foreign substances, such as bacteria and viruses, and neutralises them. After exposure to a foreign substance, called an antigen, antibodies remember that antigen and act quickly if the body is exposed to it again.
- **Antigen:** a molecule, such as a toxin or foreign substance which is recognised by the immune system and can stimulate an immune response.
- **Antioxidant:** a substance that can prevent, or slow, damage to cells caused by free radicals –unstable substances which the body produces in response to environmental or other stressors such as infections, smoking, pollution and unhealthy diets.
- **Cytokines:** signaling proteins released by white cells which regulate immunity.
- **Gut microbiota:** all the micro-organisms – bacteria, viruses and fungi – found in the gut. The gut microbiota varies between individuals and at different times of life.
- **Gut microbiome:** genetic material from all the micro-organisms in the gut.
- **Hesperidin:** a type of polyphenol found in citrus peel, citrus fruits and their juices. Polyphenols are recognised for their beneficial health effects and are often described as **bioactives**. Hesperidin is 'available' to be absorbed by the body, and drinking orange juice raises blood levels of *hespiritin* (a hesperidin metabolite).
- **Immune response:** a response sparked by a substance known as an antigen (a component of an invader).
- **Immune system:** a defense system involving many biological structures – including the lining of the gut, gut microbiota, lymph nodes, thymus, spleen, bone marrow, appendix, tonsils – and processes that, together, protect against disease.
- **Influenza A:** a type of influenza virus that is a common cause of flu.
- **Interferons:** a group of proteins within the category of cytokines, made and released by host cells in response to viruses. Interferons work by causing nearby cells to increase their anti-viral activity.
- **NK cells:** natural killer cells, a type of immune cell that can kill virally infected cells (cytotoxic T cells do this too).
- **Oxidant/antioxidant balance:** vital for healthy tissues, a disruption of this causes tissue damage, known as 'oxidative stress'. Oxidant/antioxidant balance is maintained by consuming antioxidants from the diet e.g. vitamin C, polyphenols.
- **Reactive oxygen species (ROS):** produced during normal metabolic functions in the body and in response to external stimuli e.g. stress, pollution, smoking but can be damaging to the body.
- **T cells:** also called T lymphocytes, a type of white blood cell that seeks out and destroys pathogens that carry antigens.
- **Virus:** a sub-microscopic infectious agent that can only replicate inside the living cells of an organism, called the 'host'.

SECTION 1:

UNDERSTANDING IMMUNITY

INTRODUCTION

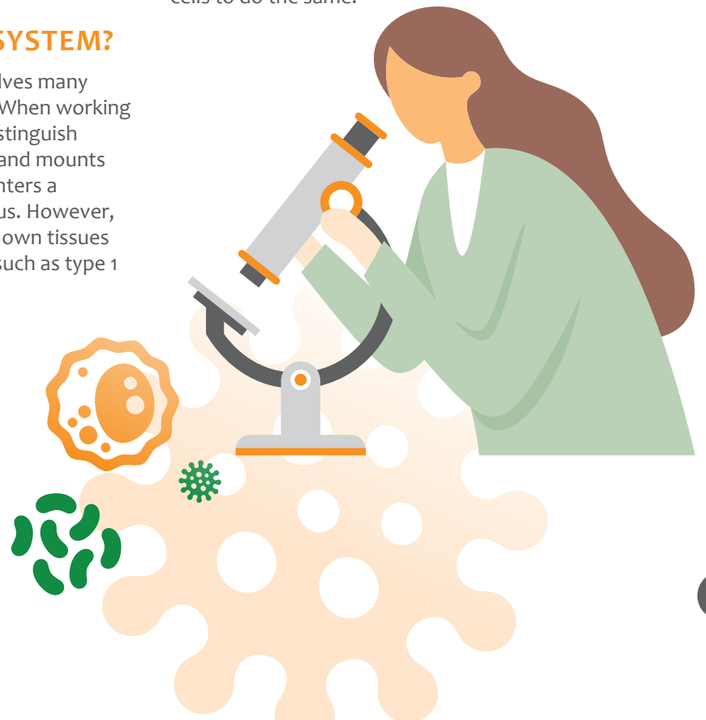
The immune system is essential for our survival, keeping us healthy and reducing our risk of infections. With no immune system our body would be open to attack from disease-causing (pathogenic) microbes, including bacteria, viruses, fungi and parasites.

WHAT IS THE IMMUNE SYSTEM?

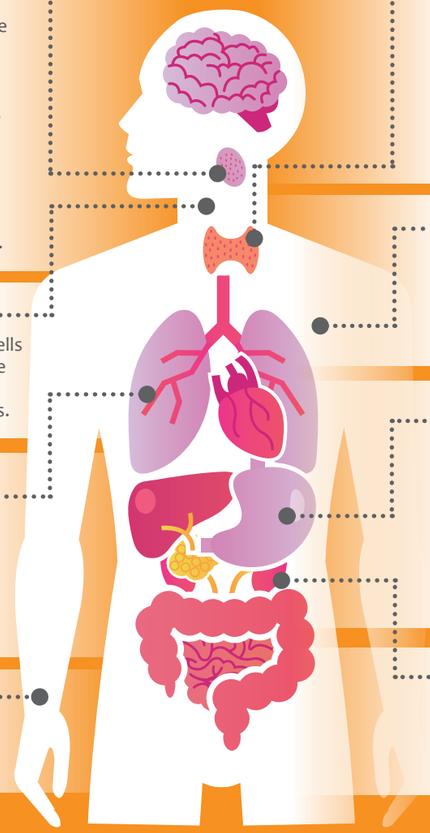
Spread throughout the body, it involves many types of cells, organs, and proteins. When working properly, the immune system can distinguish our own cells from external threats and mounts an immune response when it encounters a pathogen such as a bacterium or virus. However, an overactive system can attack our own tissues leading to autoimmune conditions, such as type 1 diabetes and multiple sclerosis.

CELLS OF THE IMMUNE SYSTEM

White blood cells (leukocytes) are the main type of immune cells and can be found circulating in blood and lymphatic vessels. Leukocytes are constantly on the lookout for pathogens. When they find a target, they multiply and signal to other immune cells to do the same.



THE BODY'S IMMUNE DEFENSE SYSTEM:



ADENOIDS

Adenoids are a patch of tissue that is high up in the throat, just behind the nose. They, along with the tonsils, are part of the lymphatic system. The lymphatic system clears away infection and keeps body fluids in balance. The adenoids and tonsils work by trapping germs coming in through the mouth and nose.

LYMPH NODES

In the lymph nodes are the cells (lymphocytes) of the immune system. These recognise and eliminate invading pathogens.

RESPIRATORY SYSTEM

The Cilia (fine hair-like projections) line the airway and move mucus and contaminants upwards out of the repiratory tract.

SKIN

The skin forms a very effective barrier against invading pathogens.

THYMUS GLAND

The thymus glad trains and differentiates T cells into specialised categories. This includes Cytotoxic T cells, T helper cells and T regulatory cells.

WHITE BLOOD CELLS

How white blood cells attack pathogens both in the blood itself and in other tissues of the body.

STOMACH AND INTESTINES

Stomach acid kills most harmful bacteria. Antibodies secreted by the intestinal cells attack viruses and other pathogens that have landed in the intestinal tract.

SPLEEN

The spleen assists the body in protecting itself against bacterial infections.

WHAT IS AN IMMUNE RESPONSE?

An immune response is a reaction sparked by a substance known as an antigen - put simply, an invader. Initially, a range of immune cell types work together to recognise the antigen as an invader by detecting and assessing proteins that are found on the surface of all cells.

Every stage of the immune response is reliant on certain micronutrients. Vitamin C was the first micronutrient to be recognised for its role in immunity. Several others are now known to be important for the immune response – see Section 2.

HOW WE FIGHT BACTERIA AND VIRUSES

The immune response to bacteria and to viruses is somewhat different.

- **Bacteria**. Our bodies and environment are covered with bacteria. Skin and internal mucous membranes in the mouth, nose, eyes and gastrointestinal tract act as physical barriers to prevent infection. When the skin or mucous membranes are damaged due to disease, inflammation or injury, bacteria can enter the body. Bacteria can then be recognised by the immune system and if harmful will be destroyed.
- **Viruses**. We are frequently exposed to viruses, which can only survive and multiply when they get inside our cells. This allows them to "hide" from our immune system. However, when a virus infects a cell, the cell releases cytokines to alert other cells to the infection. This "alert" helps to prevent other cells from becoming infected.

THE WORLD OF LEUKOCYTES

How our immune system works and protects itself is governed by a network of cells that communicate and defend. There are two main types of leukocytes:

- **Lymphocytes.**
- **Phagocytes.**

Lymphocytes – help the body to recognise and remember invaders. There are three types: B lymphocytes, T lymphocytes, and Natural Killer (NK) cells.

B lymphocytes (B cells) – spot the antigen (invader) and generate antibodies specific to that antigen.

T lymphocytes (T cells) – attack cells infected with viruses. They also regulate the immune system in the same way that a conductor leads an orchestra.

Natural killer (NK) cells – destroy virus-riddled cells by injecting toxic chemicals into them. They are also vital in defending against some cancers.[6]

Phagocytes – surround and absorb pathogens. There are several types. See Appendix 1 for more details.

WHAT IS IMMUNITY?

Once an antibody has been produced, a copy remains in the body so that, if the same antigen returns, it can be dealt with more quickly. This is called immunity.

TYPES OF IMMUNITY:

Innate immunity:
We are all born with some level of immunity so our immune system can deal with invaders from day one. In young children, early immunity is related to IgM (immunoglobulin – type of antibody) and the barriers provided by the skin and mucous membranes of the throat and gut.[7]

Adaptive immunity:
This develops as we are exposed to diseases or get vaccinated, and we build up a library of antibodies to different pathogens, sometimes called 'immunological memory'. These responses involve mature T cells and B cells that require training not to attack our own cells.

Passive immunity:
This is 'borrowed' and does not last indefinitely. A baby receives antibodies from their mother through the placenta before birth and in breast milk following birth. This protects them from some infections during their early years.

GUT REACTION: HOW OUR FRIENDLY GUT BACTERIA PROTECT US

The human intestine is colonised by trillions of micro-organisms from 300-500 species. Most are harmless bacteria that have co-evolved with us in a symbiotic relationship. The collection of microbes that live in the intestine is known as the gut microbiota.[8]

A principal function of the microbiota is to protect the intestine against colonisation by invader pathogens and potentially harmful microorganisms, including bacteria, viruses, fungi and parasites.

Diet plays a key role in the health of the gut microbiota. Eating plenty of plant-based foods, which are rich in polyphenols, such as fruit, vegetables and fruit juice, as well as high fibre foods can positively impact gut bacteria.

The gut microbiota and immune system are mutually dependent – each influences the other. This inter-dependence is why 70-80% of the body's immune cells are found in the wall of the gut.

Under normal conditions, the immune system promotes the growth of beneficial microbes and helps maintain a stable microbial community. In return, a healthy microbiota produces molecular signals that support the development of immune cells and help fine-tune our immune response. Breakdown of, or imbalances in, the normal microbial community disrupts the gut barrier and increases the risk of pathogen invasion, infection or the overgrowth of normally harmless bacteria.

SUMMARY

The immune system is complex and spread throughout the body. Its function is to detect and destroy invaders – such as a virus or bacterium. The gut microbiota, which is influenced by what we eat and drink, play a key role in our immune health and wellness. Vitamin C, folic acid and vitamin D as well as trace elements and plant-based polyphenols found in fruit, vegetables and fruit juices, help optimise the immune function.

SECTION 2:

IMMUNE HEALTH AND NUTRITION

INTRODUCTION

Nutrition has a well-established role in immune health. Several vitamins including vitamins A, B6, B12, C, D, E and folate; and trace elements and minerals including zinc, iron, selenium and copper play essential and complementary roles in both innate and adaptive immunity.[9,10]

So, why are nutrients so important? Adequate amounts of vitamins and minerals are vital to ensure the proper function of immune cells, as well as the physical barriers of the skin and mucous membranes.

NUTRIENT DEFICIENCIES

Deficiencies and suboptimal levels of nutrients can have a negative impact on immune function and lower resistance to infection. Nutrients, such as omega-3 fatty acids, contribute to our immune health by helping to manage the inflammatory response. Substances impacting on the gut microbiota, such as the polyphenols - hesperidin and quercetin - and prebiotics and probiotics also play a key role in immunity.

Worryingly, a proportion of the German population have intakes of micronutrients below recommended intakes, which puts them at risk of deficiency. However, even marginal deficiency may impair immune function because micronutrient requirements increase when our bodies are dealing with infection, stress, pollution and other pressures. This leads to further reductions in micronutrient stores and a potential impact on immune health.

NUTRIENTS SUPPORTING OUR IMMUNE FUNCTION

Nutrients regulate both innate and adaptive immunity. In the following section of this report we examine five nutritional heroes of the immune system. See Appendix 2, Table 1, pages 35-36 for further information on which vitamins, minerals and trace elements support immune function and how they do this.

FRUIT JUICE SCIENCE CENTRE FACT:

Vitamin C, also called ascorbic acid, is a water-soluble, anti-oxidant vitamin present in foods including citrus fruits, citrus and other fruit juices, tomatoes, red and green peppers, kiwi fruit, strawberries, broccoli and potatoes.

FIVE FUNDAMENTAL IMMUNE HERO NUTRIENTS

Most nutrients have a role in immune support, but five are amongst those that are most important:

- **Vitamin C**
- **Vitamin D**
- **Folate**
- **Omega-3 fatty acids**
- **Gut modulators** (polyphenols, prebiotics and probiotics)

From scurvy to immune hero

More than half a century of research has identified the multiplicity of roles played by vitamin C in the immune system. Severe vitamin C deficiency causes scurvy – once a common killer on long sea voyages. Citrus fruits were known to cure scurvy as long ago as the 15th century, but it was not until 1747, when Lind (James Lind – remembered as the man who helped to conquer the killer disease - scurvy) conducted one of the world's first controlled experiments and discovered that citrus fruits prevented the disease. Vitamin C itself was not discovered until 1912.

FRUIT JUICE SCIENCE CENTRE FACT:

Scurvy results in poor wound healing and impaired immunity with a high risk of potentially fatal infections like pneumonia.

How much vitamin C is needed?

The recommendation is 80 mg a day but scientists have found that intakes of around 200 mg a day are required for optimal blood levels in healthy individuals.[11] The German National Nutrition Survey indicates that mean intakes of vitamin C are 109mg daily.[12] Vitamin C is important for ensuring maximum antioxidant protection against free radicals – loose electrons that can attack our body's cells and cause damage.[13] It's been estimated we need around 100-200 mg of antioxidants for daily health and immune wellness.

Due to the low storage capacity in the body for water-soluble vitamins, we need a regular supply of vitamin C to top up blood levels – more so during bouts of infection since this depletes vitamin C levels.

BEWARE: According to research from the Fruit Juice Science Centre most Germans are unaware of the vital need to consume vitamin C regularly. In fact, more than half (52%) believe that the body stores vitamin C and as long as you consume lots on one day, your body will be replete on the next which it will not be.

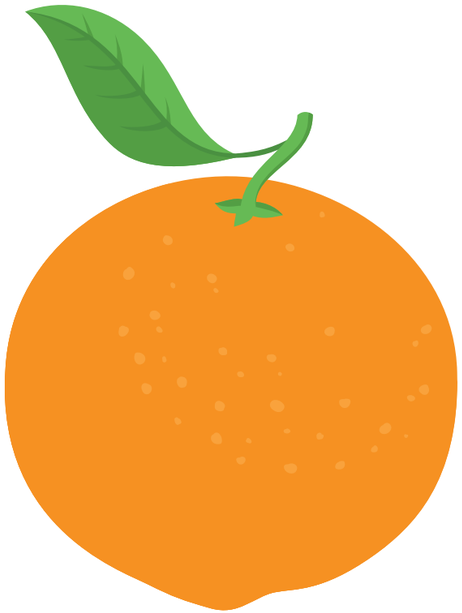
Deficiency risks?

A report by the German Nutrition Society indicates that mean intakes of vitamin C across the population fulfil recommended intakes, but low intakes are evident in young children and in people over the age of 65 where vitamin C intakes are approximately half of reference values.[14] In a study of 188 adults in Germany,[15] 17.4% had inadequate vitamin C, and levels indicative of deficiency were found in 6%.

WHY ARE WE SHORT OF VITAMIN C?

Vitamin C is derived primarily from fruits and vegetables. German Nutrition Society data show that intake of fruit and vegetables approximates to 270g daily.[16] This is considerably lower than the 400g daily fruit and vegetable intake recommended by the World Health Organization (WHO).[17]

A 150ml glass of 100% fruit juice provides 67.5mg of vitamin C and could boost vitamin C intakes across the population. Yet only 19% of Germans drink 100% fruit juice daily whilst 36% drink it a few times a week.



Vitamin C role in immunity

Vitamin C supports immunity in a host of ways including:

- Supporting physical barrier function (skin and mucous membranes).
- Growth and function of innate and adaptive immune cells.
- White cell movement to sites of infection
- Antibody production and killing of microbes.

Vitamin C levels in white blood cells – which are key immune system cells – are 10-100 times higher than in blood plasma.[18] This indicates that vitamin C is really important to the immune system.

Vitamin C influences the function of immune cells such as neutrophils – which are types of phagocytes (see Section 1 and Appendix 1). Laboratory studies show vitamin C can impact the production of interferon - an immune cell protein which inhibits virus replication and promotes production of T-lymphocytes.[19,20,21,22] Vitamin C also possesses anti-inflammatory activity.[23,24]

As vitamin C is an antioxidant, its effects are amplified when oxidative stress is increased. ‘Oxidant-antioxidant’ balance is an important element of immune function, and immune cells are particularly sensitive to changes in this balance.[25]

Oxidative damage attacks cell membranes and adversely affects signaling within, and between, different immune cells.

Many types of infections activate the phagocytes (a type of immune cell). This increases production of reactive oxygen species (ROS) which are involved in processes that deactivate viruses and kill bacteria.[26] However, many of the ROS can also be harmful to host cells (cells inside which a virus or bacteria replicates) and, in some cases, could exacerbate infections in the short term.[27,28]

Vitamin C has powerful antioxidant effects which protect host cells from ROS released in response to infection.

Impact of vitamin C as an anti-viral agent

Vitamin C's potential role as an anti-viral substance stems from its antioxidant activity and positive effects on immune cells. Vitamin C also has a role in collagen synthesis which stabilises the barriers of cells protecting the respiratory tract, skin and gut.

A laboratory study found that vitamin C inhibited replication of viruses from three different families:

- Herpes simplex virus type 1 (HSV-1)
- Influenza virus type A
- Poliovirus[29]

Studies show vitamin C reduces lung inflammation caused by viral infection[30] and boosts the production of interferon – naturally – during the early stages of infection with the influenza A virus.[31]

VITAMIN D

A fat-soluble nutrient, vitamin D is found in small amounts in only a few foods – primarily oily fish, eggs, butter, milk, liver, fortified cereals and spreads. From the age of four we need around 10 micrograms daily.

Most of the vitamin D in the body is created in response to sunlight on the skin but it's clear that sunshine levels in Germany are inadequate for many since a significant proportion of the population has insufficient blood levels.

In a study conducted between 2008 and 2011, more than half of Germans (61.6%)[32] (63% of 1-17 year olds; 57.3% of 18-79 year olds[33]) had vitamin D blood levels below the common threshold of 50 nmol/litre whilst 30.2% had levels <30 nmol/l. During summer, half of the participants had levels >/=50 nmol/l, whilst during winter time, 25% of the participants had levels <30 nmol/l.[34]

While the role of vitamin D in the health of bones and muscles is well known, more recent studies have found vitamin D receptors on several types of immune cells.[35]

Low vitamin D levels in blood increase the risk of respiratory tract infections.[36] A systematic review of observational studies found an increased risk of upper and lower respiratory tract infections when children had low serum vitamin D levels.[37] And a meta-analysis of 25 studies found supplementation with vitamin D reduced the risk of respiratory tract infections.[38]

FOLATE

Folate is a water-soluble B vitamin vital for our cell health as it's needed to make DNA and other genetic materials. Lack of folic acid during pregnancy is associated with neural tube defects (NTDs) such as spina bifida. Folate is also essential for the immune system, including antibody production and function.

Foods containing folate are:

- Whole fruit and fruit juice (particularly oranges and orange juice)
- Nuts, seeds, beans and peas
- Green leafy vegetables (e.g. asparagus, Brussels sprouts, spinach and kale)

We need roughly 200 micrograms daily with mums-to-be advised to supplement their diets with an additional 400 micrograms daily.

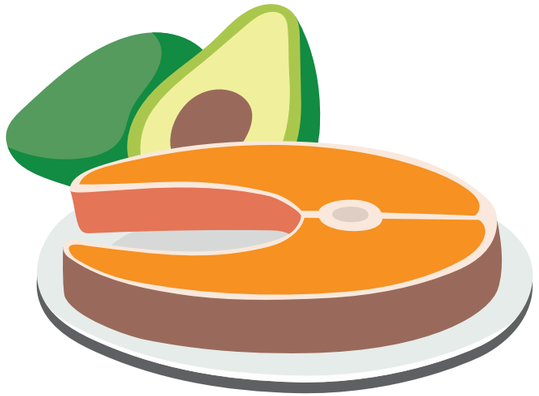
Folate intake in Germany is low and folate deficiency is common; the median intake of folate equivalents in Germany is 283 micrograms daily for men and 252 micrograms daily for women.[39] The recommended dosages are 400 micrograms daily and, for pregnant women 600 micrograms daily.

OMEGA-3 FATTY ACIDS

Omega 3 fatty acids target and reduce body inflammation,[40] but not one person surveyed by the Fruit Juice Science Centre linked omega-3s with immune function.

Low blood levels of omega-3s have been found in Germany.[41] A study in 446 middle aged German women (40-60 years) found that almost two thirds (62.8%) had a low omega-3 level.[42] Low omega-3 levels have also been found in German athletes.[43]

The long chain omega-3 fats, DHA and EPA, are mostly found in oily fish such as sardines, salmon and tuna.



GUT HEALTH MODULATORS

These are the fifth group of immune system heroes. Shifting the gut microbiota in a healthy direction can support immune function by strengthening the gut barrier and crowding out or repelling any potential pathogens that make their way into the gut from our environment (see Section 1).

Studies show that traditional fermented foods, such as yoghurt, pickles, miso, kefir and sauerkraut – as well as modern probiotics drinks and supplements – encourage bacterial diversity and help promote 'friendly bacteria'. Encouraging Bifidobacteria and Lactobacilli species and inhibiting potential pathogens, like Helicobacter and E. coli, is the goal of gut modulation.[44] Many prebiotics are high in fibre and non-digestible carbohydrates, such as inulin and galacto-oligosaccharides, which interact with the gut bacteria and encourage more favourable species to thrive.

Emerging research suggests that ß-cryptoxanthin, a bioactive substance in orange juice, can also influence immune function.[48] ß-cryptoxanthin is converted to the active form of vitamin A which is a well-established modulator of immune function.

PLANT POLYPHENOLS – THE NEW PREBIOTICS

New evidence suggests that plant polyphenols found in fruit juices and tea can also interact with the gut microbiota. Citrus juices, for example, contain a polyphenol called hesperidin which has been shown to have prebiotic effects.[45]

- Laboratory research has revealed positive gut immune changes following hesperidin administration,[46] including positive changes to the gut microbiota such as a higher proportion of *Lactobacillus*
- An increase in IgA (antibody blood protein that's part of your immune system) in the small intestine – which repels pathogens
- An increased proportion of lymphocytes in gut wall lymph nodes.[47]

SUMMARY

Vitamin C, folate, vitamin D, omega-3 fatty acids and plant polyphenols, including the citrus flavanone, hesperidin, and the pro-vitamin A carotenoid, β-cryptoxanthin, help keep our immune system healthy. Orange juice provides a convenient and valuable source of vitamin C and folate as well as the bioactive compounds, hesperidin and carotenoids (β-cryptoxanthin). These bioactive ingredients are highly bioavailable (absorbed and available for utilisation by the body) from 100% fruit juice.

SECTION 3:

FRUIT JUICE AND IMMUNE SUPPORTING NUTRIENTS

INTRODUCTION

Everyone knows oranges and other citrus fruits are rich in vitamin C, but what about orange juice?

More than four in ten (43%) Germans polled by the Fruit Juice Science Centre confirmed they drink fruit juice for its vitamin C content which is no surprise as the most commonly consumed juice, orange juice, is rich in vitamin C and provides 80-100% of the recommendation per glass. What is less well known is that orange juice contains folate and polyphenols, specifically the citrus flavanones:

- Hesperidin
- Naringin
- Narirutin

Orange juice also provides carotenoids, including lutein and zeaxanthin,[49] and the vitamin A precursor - ß-cryptoxanthin.[50] In the Fruit Juice Science Centre survey, 57% of respondents had not heard of polyphenols despite the scientific literature being awash with studies about the vascular and cognitive health benefits of these.

The Fruit Juice Science Centre survey found that 81% of adults in Germany drink fruit juice sometimes, 36% drink it a few times a week, while only 19% claimed to drink it daily.

NUTRITION IN A GLASS

On average, a typical small glass of orange juice (150 ml) provides 67.5 mg of vitamin C, which is more than 80% of the Nutrient Reference Value – set at 80 mg daily for health maintenance. A serving also provides 16% of the NRV for folate, a nutrient that supports normal immunity, and 13% of the NRV for potassium, a mineral which is vital for normal blood pressure.

WHAT'S IN A GLASS OF 100% ORANGE JUICE?

	100 ml	150 ml	200 ml
Energy (kcal)	41	62	82
Total sugars (g)	9	14	18
Vitamin C (mg)	45	67.5	90
Folate (mcg)	21.5	32.3	43
Potassium (mg)	176	264	352
Hesperidin (mg)	52	78	104
Total carotenoids (mg)	0.7	1.1	1.4
Pectins (mg)	33.4	50.1	66.8

Chart source: Data from SGF International (2018) and other sources; 1-2 medium sized oranges per glass of 100% orange juice based on public calculations from Tetrapak.[51]

100% orange juice contains vitamin C, folate and potassium which provide a range of vital wellness and immune benefits:

Vitamin C	Folate	Potassium
Increases iron absorption	Helps normal psychological function	Supports the maintenance of normal blood pressure
Helps the immune system to work normally	**Helps the immune system to work normally**	Helps muscles to work normally
Helps protect cells from oxidative stress	Has a role in the process of cell division	Contributes to the normal functioning of the nervous system
Helps reduce tiredness and fatigue	Helps reduce tiredness and fatigue	

HESPERIDIN: WHAT IS IT?

Hesperidin, part of the Vitamin P family, is a flavanone glycoside (type of polyphenol compound). Polyphenols are bioactive compounds recognised for their health properties, especially in relation to vascular function. However, more than half (57%) of those questioned by the Fruit Juice Science Centre had not heard of polyphenols, and only 34% who had heard of them knew they are natural plant compounds.

Hesperidin is found in citrus peel and albedo (pith), citrus fruits and their juices. A typical 150 ml glass of 100% orange juice provides 78 mg of hesperidin. It is 'available' to be absorbed by the body after it has been broken down by gut bacteria in the colon. Eating oranges and drinking orange juice raises blood levels of *hesperitin* (a hesperidin metabolite).

While there is more hesperidin in whole oranges than in orange juice, we end up with similar hesperitin levels in the blood after eating them. This is probably because the fibre in whole oranges inhibits hesperidin uptake in the gut.

FRUIT JUICE SCIENCE CENTRE FACT:

Commercially produced orange juice contains three times more hesperidin than home-squeezed juice. This is because commercial juicing is more efficient at releasing hesperidin from the pith.

WHAT ARE THE BENEFITS OF HESPERIDIN?

Studies show hesperidin is an antioxidant, anti-bacterial, has lipid-lowering effects and insulin-sensitising properties. Clinical trials confirm hesperidin has a beneficial impact on cardiovascular disease risk factors, such as vascular function, raised blood pressure and inflammation.[52]

In a randomised controlled crossover trial in healthy, but overweight men aged 50-65 years,[53] volunteers consumed 500 ml of orange juice, a 500 ml control drink plus hesperidin, or a 500 ml control drink plus placebo during three 4-week periods. Both orange juice and the hesperidin drink lowered diastolic blood pressure and, when consumed after a meal, increased vascular protection. Plausible mechanisms relate to the anti-inflammatory effects of hesperidin and enhanced production of nitric oxide which helps control blood pressure.[54]

THE EMERGING SCIENCE DISCOVERY:

Covid-19 and Hesperidin

A major new discovery for 2020 is that hesperidin can bind to key proteins of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) –the virus that causes Covid-19. A recent review[55] described research showing that hesperidin locks on strongly to the infamous coronavirus "spike" protein which the virus uses to break into our cells. Not only this, modelling studies of hesperidin suggest it could inhibit the release of the main 'protease' enzyme that the virus uses to break down our cell proteins. This is a vital step stopping the virus from commandeering our own cells to make multiple copies of itself. The 'binding energy' of hesperidin – how strongly and easily it locks onto the virus – is superior to that found for some common anti-viral drugs – lopinavir, ritonavir, and indinavir, suggesting that hesperidin could be useful in medications for Covid-19.

While these studies are not directly transferable to dietary sources of hesperidin at present, it is known from other work that hesperidin and vitamin C both counteract cell damage caused by the oxygen free radicals generated by an immune response and calm inflammation. These are helpful steps in promoting recovery from infections.

BENEFITS OF CAROTENOIDS IN 100% FRUIT JUICE

100% fruit juice is a bioavailable source of several carotenoids including lutein, zeaxanthin and ß-cryptoxanthin – which is used in the body to manufacture vitamin A.

In one trial, ß-cryptoxanthin lowered total, LDL and HDL cholesterol and positively modified bone turnover markers.[56] Lutein and zeaxanthin have been found to partially restore vision in people with age-related macular degeneration.[57]

SUMMARY

Fruit juice provides a range of nutrients – notably vitamin C, hesperidin and folate – which support the immune system. Vitamin C has anti-viral activity (see section 2) and emerging evidence suggests hesperidin could improve immune functionality through a prebiotic action in the gut. Emerging evidence from modelling studies points to a potential role for hesperidin in pharmacological treatments for Covid-19.

SECTION 4:

NUTRITIONAL BIOAVAILABILITY

INTRODUCTION

Section 3 reviewed the nutrients and polyphenols in fruit juice, but the bioavailability of these nutrients is important to consider as this determines how much our bodies can absorb and use. In this section we answer three key questions:

- Why is 100% fruit juice a bioavailable source of nutrients and bioactives?
- How does it compare with whole fruit?
- How does fresh juice compare with packaged juice?

BLOOD SAMPLES SHOWED THE PARTICIPANTS' VITAMIN C AND FOLATE LEVELS INCREASED BY AROUND 50%

WHY 100% FRUIT JUICE IS A BIOAVAILABLE SOURCE OF NUTRIENTS

Research confirms that the nutrients and bioactives in 100% fruit juice are highly bioavailable. One study investigated adults who ate a low-polyphenol diet for two days before they were given 250 ml of 100% orange juice (containing 584 mmol of polyphenols, mostly as flavanones).[58] A control group was given a placebo drink. Urine sampling showed that flavanone metabolites appeared two to ten hours after consuming the juice and, based on the amounts excreted, it was clear that almost 90% had been taken up by the body.

In a three-week study,[59] adults drank 236 ml juice three times daily which provided 256 mg vitamin C, 229 mg hesperidin, 6 mg carotenoids and 160 µg folate. Blood samples showed the participants' vitamin C and folate levels increased by around 50%, while flavanone levels rose by a multiple of **eight**. Carotenoid levels increased by **22%**.

FRUIT JUICE SCIENCE CENTRE FACT:

Bioavailability is the degree to which the nutrients in food can be absorbed and used in the body.

HOW DO JUICES COMPARE WITH WHOLE FRUIT?

A randomised crossover study[60] comparing the bioavailability of carotenoids from fresh oranges versus pasteurised 100% orange juice found that one of the carotenoids (ß-cryptoxanthin) was 1.8 times more bioavailable in the juice than the whole fruit. Based on a separate laboratory method, ß-cryptoxanthin was five times more bioaccessible in 100% orange juice versus whole oranges.

The lower bioavailability of bioactives in whole fruit may be due to the higher fibre levels in fruit inhibiting absorption. Another possibility is that because juicing breaks down cell walls within the fruit, more bioactives are released.

Further research[61] examined how much of the flavanones – hesperidin and narirutin – would be absorbed from 100% orange juice compared with whole oranges.[62] Despite whole oranges containing more than twice the hesperidin levels found in100% orange juice, 24-hour urine measurements showed similar levels of hesperidin metabolites in urine. This suggests that hesperidin is absorbed more effectively from juice compared with whole oranges.

PACKAGED JUICE MAY BE BETTER THAN HOMEMADE

It's often assumed that freshly squeezed juice is nutritionally superior to commercially made fruit juice. But this isn't the case. A randomised cross-over trial where freshly squeezed and packaged 100% orange juice were given for two days – each separated by a 30-day washout – found no statistical differences in the metabolism of hesperidin and narirutin.

However, due to the higher flavanone content of packaged juice – 58 mg compared to 16 mg in the fresh juice – gut absorption and urinary excretion were significantly higher following consumption of the packaged 100% orange juice. In the Fruit Juice Centre Survey 53% of Germans said they drink packaged fruit juice from the supermarket, 24% squeeze their own at home and 24% buy juice from the supermarket refrigerator.

Overall, a glass of packaged 100% orange juice delivers three times more hesperitin in the blood than the same amount of homemade juice, but why?[63]

Flavanones are soluble compounds that are present in cell walls, juice and pith (albedo). The higher mechanical force applied during machine pressing of oranges 'pushes' more of the flavanones into the juice than we can achieve with our juicers at home.

SURPRISING HEALTH BENEFITS OF ORANGE JUICE

Studies on orange juice have revealed a range of health properties including:

- Cardiovascular benefits such as improved vascular function, lower blood pressure and even reduced blood cholesterol[64]
- Cognitive health benefits as shown in randomised clinical trials[65,66]
- Beneficial rebalancing of the gut microbiota.

Contrary to perceptions that fruit juice causes weight gain and type 2 diabetes, this is not backed by the evidence. In contrast, the benefits are becoming clearer as summarised in our 'fast facts' summary below:

Physiological Area	Health Benefit
Cardiovascular risk reduction	• Associated with reduced risk of heart disease and stroke in observational studies[67] • Contributes to **improved vascular function**[68] • Contributes to **reduced total and LDL cholesterol**[69] • Contributes to **increased HDL cholesterol and lower triglycerides**[70] • Supports **lower blood pressure**[71] • **Lowers uric acid** (risk factor for gout)[72] • **Boosts antioxidant activity**[73] • Contributes to **lower inflammation**[74]
Glycaemic control and risk of type 2 diabetes	• Orange juice has a relatively **low glycaemic index** (GI) (50) in part due to its fructose content[75] • Hesperidin slows **absorption of fruit sugars** in the gut – this explains the lower than expected glycaemic index of orange juice[76] • Regular consumption of 100% fruit juice has no **impact on glycaemic control**, insulin sensitivity or **risk of type 2 diabetes**[77]
Obesity and weight control	• No significant change in body weight and BMI when fruit juice is consumed regularly[78]
Dental Health	• Not associated with tooth erosion or dental caries in children and adolescents[79] • Not associated with early childhood caries[80]
Gut microbiota (effect of polyphenols)	• Prebiotic effect[81] • Can **increase numbers of good bacteria** (*Bifidobacterium and Lactobacillus*)[82] • Acts as substrate for gut microbes, **modulating gut microbiota composition**[83]
Cognition (effect of flavonoids)	• Can increase cognition and alertness in short-term randomised clinical trials[84]

SECTION 5:

ATTITUDES, HABITS AND WHAT WE LOVE ABOUT FRUIT JUICE

A survey of 1029 German adults, commissioned by the Fruit Juice Science Centre provides detailed insights on consumption patterns and attitudes to fruit juice.[85] In this section we take a look at people's attitudes and habits and bust a few myths around fruit juice.

FRUIT JUICE CONSUMPTION

More than three quarters (81%) of Germans drink 100% fruit juice.

- More than half (53%) drink packaged fruit juice from the supermarket chiller
- 24% drink home squeezed fruit juice
- 24% drink packaged fruit juice from the supermarket shelf.

Less than one fifth (19%) of of those surveyed drink fruit juice daily, 36% drink it a few times a week, nearly half (48%) have fruit juice with breakfast whilst 43% say they have it whenever they are thirsty.

WHY DO GERMANS DRINK FRUIT JUICE?

Apart from liking the taste (44%) and to be healthier (34%) we drink juice:

- to increase vitamin levels (38%)
- because of habit (34%)
- for refreshment (32%)

IMMUNE FUNCTION SUPPORT

Covid-19 has put immune function on people's radar with over a third of those polled (35%) reporting the pandemic has increased their awareness of the importance of their immune system. Their top 3 choices for immunity were:

1. Fruit - the most popular choice (51%)
2. Vegetables (47%)
3. Fruit juice (34%)

The Fruit Juice Science Centre survey asked which vitamins, minerals and essential fats could impact the immune system if intakes were low:

- **Six out of 10** (60%) identified vitamin C
- **More than half** (54%) mentioned vitamin D
- **41%** said magnesium

Vitamin C is especially important for immune function but respondents did not mention other nutrients of value for immune function such as folate.

FRUIT JUICE FOR IMMUNE HEALTH

In terms of specific juices, 31% of those polled said that orange juice is best for immune health. This was followed by mixed fruit juice (21%) and pomegranate juice (10%).

More than half (53%) knew fruit juice is rich in vitamins and minerals but no one knew it is high in antioxidants and polyphenols.

COVID-19 HAS PUT IMMUNE FUNCTION ON PEOPLE'S RADAR WITH OVER A THIRD OF THOSE POLLED (35%) REPORTING THE PANDEMIC HAS INCREASED THEIR AWARENESS OF THE IMPORTANCE OF THEIR IMMUNE SYSTEM

KNOWLEDGE OF THE HEALTH BENEFITS OF VITAMIN C

Our knowledge of the specific health benefits of vitamin C is patchy.

- **79%** did not realise vitamin C is good for the heart.
- **72%** did not know vitamin C helps protect cells from damage.
- **40%** had no idea vitamin C supports immune function.

FRUIT JUICE SCIENCE CENTRE FACT:

27% of Germans think we just need 50 mg of vitamin C a day but we actually need to consume 200 mg a day for optimal immune health.[86]

KNOWLEDGE OF POLYPHENOLS

Knowledge of polyphenols is even worse. Despite the growing evidence of the importance for health, more than half (57%) of people polled by the Fruit Juice Science Centre had not heard about polyphenols.

When asked about the best sources of polyphenols people noted:

- **Vegetables** (53%)
- **Berries** (38 %)
- **Olive oil** (32 %)

Responses were positive in that only plant foods – primarily vegetables, beans, fruits and their juices – provide polyphenols. Worryingly, despite all the evidence, not one of those polled identified orange juice as a dietary source rich in highly bioavailable polyphenols, such as hesperidin.

Vitamin C is water soluble, so it's excreted rapidly and you need to keep topping it up. However, 52% of those surveyed believe that a single blitz on vitamin C rich foods could keep you topped up for a few days. And 52% of Germans wrongly believe the body stores Vitamin C, ready to use when needed.

IMMUNE FUNCTION WISDOM?

Given the current pandemic, public understanding of the immune system is surprisingly vague and inconsistent.

More than three quarters (77%) of people who took part in the Fruit Juice Science Centre research knew the immune system fights viruses and bacteria. But that also means a quarter did not realise. And although viruses and bacteria are the most common cause of coughs and colds, only 53% knew we are more likely to pick up viruses when our immune system is compromised.

Despite centuries of anecdote and evidence, almost half (47%) did not realise that a shortfall of vitamin C can compromise the immune system. The most commonly perceived threats were:

- Alcohol (64 %)
- Stress (64%)

FRUIT JUICE SCIENCE CENTRE FACT:

47% of Germans are unaware that if the immune system is compromised, they are more likely to pick up viruses

SUMMARY

German people enjoy fruit juice, with 81% drinking it. However, only 19% drink fruit juice daily. Of those people who do drink fruit juice, 66% choose orange juice. The Fruit Juice Science Centre Survey found some interest in foods and drinks for the immune function in the context of the Covid pandemic. Just over half (53%) of those surveyed identified vitamin C as essential for immune health, yet fewer than a third (31%) identified orange juice, which is rich in vitamin C, as beneficial for immune wellness. Knowledge of polyphenols was poor with an absence of knowledge that fruit juice contains these healthy antioxidant nutrients. In fact, more than half of respondents (57%) had not heard of polyphenols and no one could identify fruit juice as a source of these health-promoting compounds. Knowledge of immune function was vague and inconsistent with one-third having no idea that the immune system fights viruses and bacteria. Plus, almost half (47%) did not understand that a shortfall in vitamin C can compromise immune function.
As a result, Germans need to get savvy about their immune health. That means everyone needs to ensure their bodies are well-fueled with the right nutrients.

LAST WORD:

FRUIT JUICE, HESPERIDIN AND IMMUNE HEALTH

DR GILL JENKINS, DR CARRIE RUXTON AND PROFESSOR PHILIP CALDER

With the peak virus season approaching – and the Covid pandemic continuing - it's important to eat right to stay healthy and free from illness. A simple step is to drink a daily glass of 100% fruit juice.

If everyone added just 150 ml of fruit juice to their daily diet, they would not only be one step closer to their 5-a-day fruit and veg target, but would also ensure a reliable supply of vitamin C, folate and plant bioactives like polyphenols – all of which are vital for everyday wellness and normal immune health.

Hesperidin, one of the key polyphenols in citrus fruits and juices, could help support our immune function and recovery, thanks to its antioxidant and anti-inflammatory effects. Unfortunately, our current knowledge of polyphenols, including their presence in fruit juice is practically non-existent, according to research from the Fruit Juice Science Centre.

Hesperidin's prebiotic role in the gut also contributes to a healthy immune system. Recent cutting-edge evidence suggests that hesperidin could be a worthy target of pharmacological interventions thanks to its ability to bind to the protein spike of the novel coronavirus and limit its replication. It's too early to translate this into the dietary context, however it definitely highlights that there's a lot to learn and consider when it comes to polyphenols and immunity.

Then there's the high vitamin C content of fruit juice. Although the latest research shows that people understand the connection between vitamin C and immune health, they were far less aware that a shortfall of vitamin C could actually compromise immune function.

Now more than ever, it's important that we encourage everyone to stay on top of their immune health and make sure it's fit for purpose through all seasons.

HESPERIDIN COULD BE A WORTHY TARGET OF PHARMACOLOGICAL INTERVENTIONS THANKS TO ITS ABILITY TO BIND TO THE PROTEIN SPIKE OF THE NOVEL CORONAVIRUS AND LIMIT ITS REPLICATION

STRENGTHEN YOUR IMMUNE SYSTEM IN FIVE EASY STEPS

1. FRUIT JUICE LOVE:

Drink one 150 ml portion of 100% orange juice to achieve one of your 5-A-day for fruit and vegetables, 84% of the NRV for vitamin C as well as folate, and highly bioavailable plant bioactives such as hesperidin and carotenoids.

2. GREEN UP:

Eat a daily portion of leafy green vegetables such as broccoli, cabbage, spring greens or spinach for folic acid. Remember to include leafy greens in stir-fries for a quick supper, or roast them in the oven with wholegrain rice, quinoa or barley.

3. PEPPER COLOUR:

Peppers are a good source of vitamin C. Add them to stir-fries, salads and a medley of roasted vegetables, like onions, sweet potatoes, aubergines and butternut squash.

4. WEEKLY FISH FEST:

Eat one portion of oily fish each week – salmon, sardines, tuna, mackerel or herring – for vitamin D and anti-inflammatory omega-3 fatty acids.

5. 5-A-DAY:

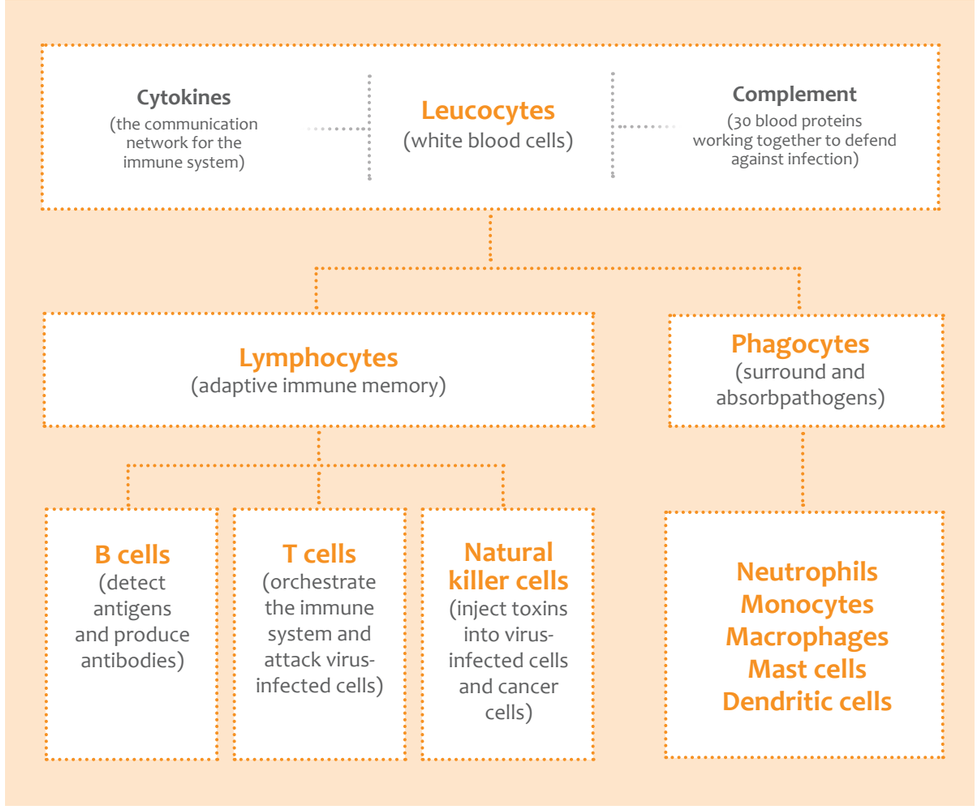
Aim for 5 portions of fruit and vegetables each day, including one glass of 100% fruit juice, for vitamin C, folate and plant bioactives. Aim for half of your evening meal plate to be vegetables. Meat, fish, and plant-based alternatives can be included as enjoyed.

APPENDIX 1: The Components of the immune system

The key organs

- **Bone marrow:** found in the centre of the bones, this is where all the cells of the immune system begin to develop. The bone marrow also produces red blood cells.
- **Thymus:** a gland between the lungs and just below the neck where some immune cells (T lymphocytes) mature.
- **Spleen:** an organ found in the upper left of the abdomen. It filters the blood and provides a space for cells and proteins from the immune system to interact and develop.
- **Lymph nodes:** small glands found throughout the body, linked by lymphatic vessels. Some immune cells (T and B lymphocytes) congregate here and communicate with each other.
- **Tonsils:** found in the throat, they collect immune cells (T lymphocytes).
- **Liver:** responsible for manufacturing proteins used by the immune system, specifically those involved in the complement system.
- **Blood:** carries cells and proteins of the immune system from one part of the body to another.
- **Gut:** acts as a physical and microbiological barrier to invading pathogens and is linked to the immune system.

THE KEY IMMUNE CELLS



Appendix 2: TABLE 1. Nutrients that support immune function

Nutrient	Function in immunity
Vitamin A	● Plays a key role in the development and differentiation of the cells of the skin barrier and mucous tissues ● Important in the defense of the oral, gut and urinary-genital mucosa ● Essential for the development and differentiation of B and T cells
Vitamin B6	● Involved in intestinal immune regulation ● Important for lymphocyte activity, mediating lymphocyte migration into the intestine ● Maintains or enhances Th1-mediated immune response ● Inhibits Th2 mediated cytokine-mediated activity ● Required for the production of antibodies
Vitamin B12	● Important for the gut barrier ● Facilitates production of T cells and helps to regulate balance between T helper cells and T killer (cytotoxic) cells ● Important for antibody production and metabolism
Folate (folic acid)	● Essential for the survival of regulatory T cells in the intestine ● Supports Th-1 mediated response ● Important for antibody production and metabolism
Vitamin C	● Protects cell membranes from ROS ● Involved in the production, development and movement of T lymphocytes, particularly cytotoxic T cells, phagocytes (monocytes and neutrophils) and NK cells ● Increases generation of antibodies, enhances killing of microbes and reduces tissue damage

Appendix 2: TABLE 1. Nutrients that support immune function[87]

Nutrient	Function in immunity
Vitamin D	• Helps to modify the gut microbiota towards a healthier composition • Protects the lungs against infection. • Vitamin D receptors are found in monocytes, macrophages and dendritic cells • Regulates proteins that kill pathogens • Reduces activity of pro-inflammatory cytokines and increases activity of anti-inflammatory cytokines • Contributes to innate and adaptive immunity
Vitamin E	• Protects cells against free radicals and inflammation • Supports the skin and gut barrier and mucous membrane barriers • Enhances lymphocyte production and T cell-mediated functions
Iron	• Essential for development and growth of skin and gut barrier and mucous membranes • Involved in killing of bacteria by neutrophils • Component of enzymes critical for function of immune cells • Involved in cytokine production and inflammatory response
Zinc	• Helps to maintain integrity and function of the skin barrier and mucous membranes • Promotes the killing activity of phagocytes
Copper	• Intrinsic antimicrobial properties • Defense against ROS and free radicals • Involved in the function of T cells (helps to regulate balance between T helper and T killer cells), macrophages, monocytes and neutrophils • Important role in inflammatory response
Selenium	• Important for antioxidant defense system, counteracting ROS • Regulates T cell and cytokine production • Involved in antibody production
Magnesium	• Involved in the regulation of leukocytes and antigen binding to macrophages • Involved in antibody production.

APPENDIX 3: Authorised health claims for nutrients and immune function[88]

Nutrient or food ingredient	Authorised health claims
Vitamin C	• Contributes to the normal function of the immune system. Daily recommendation from the diet is 80 mg • Contributes to maintain the normal function of the immune system during and after intense physical exercise (at intakes of 200 mg per day)
Vitamin D	• Contributes to the normal function of the immune system. Recommendation is to consider a daily supplement of 10 micrograms on top of summer sun exposure and dietary sources.
Folate	• Contributes to the normal function of the immune system. Daily recommendation from the diet is 200 mcg but women planning a pregnancy are advised to supplement with an additional 400 mcg daily.

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