Beyuna Flx

Content: Page:

Introduction:

The following information is solely put together for those who would like to get more information about the ingredients of the Beyuna Flx product. This work is not meant for publication or marketing purposes, just solely for individual education.

This information is not put together by Beyuna, the company, but by me (André van Commenée) for my own education as a distributor of Beyuna.

Following is a disclaimer: these statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Most information is gathered from nih.gov (National Institute of Health), WebMD, healthline.com, and other sources.

Claims:

Beyuna Flx contributes to normal collagen formation for normal function of bones.

Beyuna Flx contributes to normal collagen formation for the normal function of blood vessels

Glucosamine reduces inflammation

Supports healthy joints

Collagen Type II:
Improves skin health
Relieves joint pain
Prevents joint loss
Boosts muscle mass
Promotes heart health

Hyaluronic Acid:
Promotes Healthier, More Supple Skin
Speeds Wound Healing
Relieves Joint Pain by Keeping Bones Well Lubricated
Soothes Acid Reflux Symptoms
Relieves Dry Eye and Discomfort
Preserves Bone Strength
Prevents Bladder Pain

MSM (Methyl Sulphonyl Methane):
Lessen inflammation

Acerola Extract:
The health benefits of acerola are due to its vitamin C content.

Curcumine C3 complex®:
The Safest and The Most Versatile Phytonutrient
Strong natural anti-oxidant

Chondroitin Sulfate:
Helps rebuild cartilage naturally and boosts recovery of tissue after injury or exercise.

1 capsule of Beyuna Flx contains:

- N-Acetyl Glucosamine 250 mg
- Hydrolyzed Collagen Type II with 10% Hyaluronic Acid 250 mg
- MSM, Methyl Sulphonyl Methane 125 mg
- Acerola extract 17% 88.24 mg
- Curcumin extract, 95% Curcumin 78.95 mg
- Chondroitin Sulfate 55.56 mg
- Conventional Nu-RICE 9.25 mg
- Vitamin C (Acerola extract 17%) 15 mg

Recommended Daily Amount For Adults 2 Capsules.
Beyuna Flx has no fillers, binders or other additives, and is GMO Free.

Usage:

Take two tablets per day with a glass of water during a mean.
One tablet with breakfast and one tablet with the evening meal.
Do not exceed the recommended daily dosage.
A dietary supplement is not a substitute for a varied diet.
A healthy lifestyle and a varied, balanced diet is vital to maintaining good health.

Storage Recommendations:

Dark, closed, cool and out of the reach of young children.
Not to be used during pregnancy or breastfeeding.

What makes Beyuna FLX work so well?

If you are middle-aged or older and you struggle with joint pain and stiffness, Beyuna Flx is a great product for you.

As shared before, Beyuna Flx contributes to regular collagen formation for the normal function of bones, cartilage, and blood vessels.

Beyuna Flx contains natural vitamin C in the form of Acerola Extract. It also consists of N-Acetyl Glucosamine, Collagen Hydrolysate Type II with 10% Hyaluronic Acid, MSM, Curcumin, Chondroitin Sulfate and Conventional Nu-RICE.

Many people just want to try a product, but some people like to know the "ins-and-outs" of a product. Following is information for those who want to understand much more about the product FLX.

"It's all about quality (the amount of absorption and effectiveness) and safety." But everybody is saying that.

"Beyuna FLX meets the highest quality standards using the latest scientific insights and technological developments." But everybody is saying that too.

So what is the difference?

The truth is that there are general and specific reasons why Beyuna FLX is the best for your joint health.

A) General Reasons (Oversight/Accountability):

Beyuna FLX Quality and safety are guaranteed by:

1. applying **EHPM** rules. The European Federation of Associations of Health Product Manufacturers represents specialist health product manufacturers in Europe. Quality and safety are guaranteed by following the EHPM (European Federation of Health Products Manufacturers Associations) rules and instructions written in the Quality Guide for Food Supplements. See **www.ehpm.org**

2. following the **EFSA** (European Food Safety Authority) rules and regulations. This is the equivalent of the American Food and Drugs Administration (F.D.A.). **All statements** regarding the products are based on claims approved by the **EFSA** (European Food and Safety Authority). See **www.efsa.europa.eu**

3. following the instructions described in the **Quality Guide for Food Supplements.** See **www.ehpm.org/ehpm-standards/quality.html**

4. selecting suppliers that comply with **HACCP** (Hazard Analysis Critical Control Points). See **www.haccpalliance.org**

5. having its products analyzed by the **NZVT** (Netherlands Security System Nutritional Supplements Elite Sports) to ensure they comply with anti-doping (PEDs: Performance Enhancing Drugs) regulations. **www.dopingautoriteit.nl/ english**

6. abiding by the **FDA** regulations. Although the FDA does not approve supplement products, they do have strict regulations regarding safety, accurate and truthful product labeling, manufacturing facility registration, and Dietary Supplement Current Good Manufacturing Practices (CGMPs) for quality control. See **http://fda.gov**

7. **Z-Index**

All products are registered with **Z-Index**, the medium in the Netherlands in healthcare information regarding all health products that can be obtained by healthcare providers such as pharmacists, physicians, hospitals, etc. See https://www.z-index.nl/english

8. NPN

Beyuna is a member of the **NPN.** NPN is the branch association for producers, raw material suppliers, wholesalers, importers and distributors of nutritional supplements. See http://www.npninfo.nl/

9. GMO-Free

GMOs (or "genetically modified organisms") are organisms whose genetic material has been artificially manipulated in a laboratory through genetic engineering, or GE. This relatively new science creates unstable combinations of plant, animal, bacteria and viral genes that do not occur in nature or through traditional crossbreeding methods. For consumers, it can be difficult to stay up-to-date on food ingredients that are at-risk of being genetically modified, as the list of at-risk agricultural ingredients is frequently changing. As part of the Non-GMO Project's commitment to informed consumer choice, we work diligently to maintain an accurate list of risk ingredients. **www.nongmoproject.org**

A) FDA

www.fda.gov/Food/DietarySupplements
fnic.nal.usda.gov/dietary-supplements

FDA regulates both finished dietary supplement products and dietary ingredients. FDA regulates dietary supplements under a different set of regulations than those covering "conventional" foods and drug products.

Under the Dietary Supplement Health and Education Act of 1994 (DSHEA):

- Manufacturers and distributors of dietary supplements and dietary ingredients are prohibited from marketing products that are adulterated or misbranded. That means that these firms are responsible for evaluating the safety and labeling of their products before marketing to ensure that they meet all the requirements of DSHEA and FDA regulations.
- FDA is responsible for taking action against any adulterated or misbranded dietary supplement product after it reaches the market.

Ensuring the Safety and Accurate Labeling of Dietary Supplements
Although dietary supplement manufacturers must register their facilities with FDA,* they are not required to get FDA approval before producing or selling dietary supplements. Manufacturers and distributors must make sure that all claims and information on the product label and in other labeling are truthful and not misleading.

Under FDA regulations at 21 CFR part 111, all domestic and foreign companies that manufacture, package, label or hold dietary supplement, including those involved with testing, quality control, and dietary supplement distribution in the U.S., must comply with the Dietary Supplement Current Good Manufacturing Practices (CGMPs) for quality control.

In addition, the manufacturer, packer, or distributor whose name appears on the label of a dietary supplement marketed in the United States is required to submit to FDA all serious adverse event reports associated with use of the dietary supplement in the United States.

FDA regulates dietary supplement labels and other labeling, such as package inserts and accompanying literature. The Federal Trade Commission (FTC) regulates dietary supplement advertising.

**Domestic and foreign facilities that manufacture, process, pack, or hold food for human or animal consumption in the United States are required to register with FDA.*

B) EFSA

www.efsa.europa.eu/en/topics/topic/supplements

The EFSA is the European Food Safety Authority.

Food supplements are concentrated sources of nutrients or other substances with a nutritional or physiological effect, whose purpose is to supplement the normal diet. Food supplements are marketed 'in dose' form, for example as pills, tablets, capsules or liquids in measured doses etc. Supplements may be used to correct nutritional deficiencies or maintain an adequate intake of certain nutrients. However, in some cases excessive intake of vitamins and minerals may be harmful

or cause unwanted side effects; therefore, maximum levels are necessary to ensure their safe use in food supplements.

EU regulatory framework

The European Commission has established harmonized rules to help ensure that food supplements are safe and properly labelled. In the EU, food supplements are regulated as foods and the legislation focuses on vitamins and minerals used as ingredients of food supplements.
The main EU legislation is Directive 2002/46/EC related to food supplements containing vitamins and minerals.

The Directive sets out labelling requirements and requires that EU-wide maximum and minimum levels are set for each vitamin and mineral added to supplements. As excessive intake of vitamins and minerals may result in adverse effects, the Directive provides for the setting of maximum amounts of vitamins and minerals added to food supplements. This task has been delegated to the Commission and is currently ongoing.

EFSA's role and activities

EFSA was asked by the European Commission to evaluate the safety and bioavailability of nutrient sources proposed for addition to the list of permitted substances in Annex II of the food supplements Directive. In July 2009, EFSA completed the first comprehensive assessment of substances used as sources of vitamins and minerals in food supplements, which are currently sold in the EU.

Based on EFSA's work, the European Commission reviewed the list of permitted vitamin or mineral substances that may be added in food supplements.

Between 2005 and 2009 EFSA examined a total of 533 applications. Of these, 186 applications were withdrawn during the evaluation process, and EFSA received insufficient scientific evidence to be able to assess around half of the remaining applications. Possible safety concerns were identified in relation to 39 applications.

The evaluations were carried out by the Panel on food additives and nutrient sources added to food (ANS). The Panel's evaluations involved judging the safety of a nutrient substance at the intake levels suggested by the applicant based on best scientific knowledge available. The Panel also assessed the bioavailability of the nutrient from the source, which is the effectiveness with which the mineral or

vitamin is released from the source into the tissues of the body. Previously the former Panel on food additives, flavourings, processing aids and materials in contact with food (former AFC) was responsible for this work.

Moreover, EFSA's NDA Panel has preformed a comprehensive evaluation of the possible adverse health effects of individual micronutrients at intakes exceeding the dietary requirements and, where possible, established Tolerable Upper Intake Levels (ULs) for different population groups.

ULs represent the highest level of chronic daily intake of a nutrient that is not likely to pose a risk of adverse health effects to humans. The ULs defined by the NDA Panel and by the former Scientific Committee on Food (SCF) are used as a reference by the ANS Panel in its evaluations of the safety of nutrient substances added to food supplements. Throughout this work EFSA will provide support to the European Commission in establishing maximum limits for vitamins and minerals in food supplements and fortified foods.

B) Specific Reasons (Ingrediënts):

I) N-Acetyl Glucosamine:

Glucosamine is a molecule that occurs naturally within your body, but it's also a popular dietary supplement.

Most often used to treat symptoms of bone and joint disorders, it's likewise used to target several other inflammatory diseases.

What Is Glucosamine?

Glucosamine is a naturally occurring compound that is chemically classified as an amino sugar (1).

It serves as a building block for a variety of functional molecules in your body but is primarily recognized for developing and maintaining cartilage within your joints (1).

Glucosamine is also found in some animal and other non-human tissues, including shellfish shells, animal bones and fungi. Supplemental forms of glucosamine are often made from these natural sources.

Glucosamine is frequently used to both treat and prevent joint disorders, such as osteoarthritis. It may be taken orally or applied topically in a cream or salve.

Summary:

Glucosamine is a chemical compound that occurs naturally in both human and animal tissues. In humans, it helps form cartilage and is commonly used as a dietary supplement to treat joint disorders like osteoarthritis.

May Reduce Inflammation

Glucosamine is often used supplementally to treat symptoms of various inflammatory conditions.

Though glucosamine's mechanisms are still poorly understood, it appears to readily reduce inflammation.

One test-tube study demonstrated a significant anti-inflammatory impact when glucosamine was applied to cells involved in bone formation (2).

Much of the research on glucosamine involves simultaneously supplementing with chondroitin — a compound similar to glucosamine, which is also involved in your body's production and maintenance of healthy cartilage (3).

A study in over 200 people linked glucosamine supplements to a 28% and 24% reduction in two specific biochemical markers of inflammation: CRP and PGE. However, these results were not statistically significant (4).

It's worth noting that the same study found a 36% reduction of these inflammatory markers for people taking chondroitin. This result was, in fact, significant (4).

Other studies augment such findings. Keep in mind that many participants who take chondroitin also report simultaneously supplementing with glucosamine. Thus, it remains unclear if the results are driven by chondroitin alone or a combination of both supplements taken together (4).

Ultimately, more research is needed on glucosamine's role in the reduction of inflammatory markers in your body.

Summary:
The way glucosamine works in disease treatment is not well understood, but some research indicates that it may reduce inflammation — especially when used alongside chondroitin supplements.

Supports Healthy Joints
Glucosamine exists naturally in your body. One of its main roles is to support the healthy development of the tissues between your joints (1).

Articular cartilage is a type of smooth white tissue that covers the ends of your bones where they meet to form joints. This kind of tissue — along with a lubricating liquid called synovial fluid — allows bones to move freely across one another, minimizing friction and allowing for painless movement at your joints.

Glucosamine helps form several chemical compounds involved in the creation of articular cartilage and synovial fluid.

Some studies indicate that supplemental glucosamine may protect joint tissue by preventing the breakdown of cartilage.

One small study in 41 cyclists found that supplementing with up to 3 grams of glucosamine daily reduced collagen degradation in the knees by 27% compared to 8% in the placebo group (5).

Another small study found a significantly reduced ratio of collagen-breakdown to collagen-synthesis markers in articular joints of soccer players treated with 3 grams of glucosamine daily over a three-month period (6).

These results suggest a joint-protective effect of glucosamine. However, more research is needed.

Summary:
Glucosamine is involved in developing tissues crucial for proper joint function. While more studies are necessary, some research indicates that supplemental glucosamine may protect your joints from damage.

Often Used to Treat Bone and Joint Disorders
Glucosamine supplements are frequently taken to treat various bone and joint conditions. This molecule has been specifically studied for its potential to treat symptoms and disease progression associated with osteoarthritis, rheumatoid arthritis and osteoporosis.

Multiple studies indicate that supplementing daily with glucosamine sulfate may offer effective, long-term treatment for osteoarthritis by providing a significant reduction in pain, maintenance of joint space and overall slowing of disease progression (7, 8, 9, 10).

Some studies have revealed significantly reduced markers of rheumatoid arthritis (RA) in mice treated with various forms of glucosamine (11, 12).

Conversely, one human study didn't show any major changes in RA progression with the use of glucosamine. However, study participants reported significantly improved symptom management (13).

Some early research in mice with osteoporosis also shows potential for supplemental use of glucosamine to improve bone strength (14).

While these results are encouraging, more human research is needed to understand the mechanisms of and best applications for glucosamine in joint and bone diseases.

Summary:
Though glucosamine is used frequently to treat various bone and joint conditions, more research on its effects is needed.

Though broad claims are made about glucosamine's positive effects on many diseases, available research only supports its use for a narrow range of conditions. Currently, the strongest evidence supports glucosamine sulfate use for long-term treatment of osteoarthritis symptoms. That said, it may not work for everyone (15).

Research:

(1) https://pubchem.ncbi.nlm.nih.gov/compound/D-glucosamine
(2) https://www.ncbi.nlm.nih.gov/pubmed/17270442
(3) http://journals.sagepub.com/doi/pdf/10.1177/147323000803600602
(4) https://www.ncbi.nlm.nih.gov/pubmed/24738579
(5) https://www.ncbi.nlm.nih.gov/pubmed/23358550
(6) https://www.ncbi.nlm.nih.gov/pubmed/19724889
(7) https://www.ncbi.nlm.nih.gov/pubmed/26881468
(8) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5814472/
(9) https://www.sciencedirect.com/science/article/pii/S0140673600036102
(10) http://www.clinexprheumatol.org/article.asp?a=2272
(11) https://www.ncbi.nlm.nih.gov/pubmed/22434264
(12) https://www.ncbi.nlm.nih.gov/pubmed/30021375
(13) https://www.ncbi.nlm.nih.gov/pubmed/16953394
(14) https://www.ncbi.nlm.nih.gov/pubmed/22446865
(15) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5814472/

II) Hydrolysed Collagen Type II

Collagen type II contains chondroitin and glucosamine. Collagen is the most abundant protein in your body. It is the major component of connective tissues that make up several body parts, including tendons, ligaments, skin and muscles (1).

Collagen has many important functions, including providing your skin with structure and strengthening your bones (1).

In recent years, collagen supplements have become popular. Most are hydrolyzed, which means the collagen has been broken down, making it easier for you to absorb.

There are also several foods you can eat to increase your collagen intake, including pork skin and bone broth.

Consuming collagen may have a variety of health benefits, from relieving joint pain to improving skin health (2, 3).

Six science-backed health benefits of taking collagen.

1. Can Improve Skin Health

Collagen is a major component of your skin. It plays a role in strengthening skin, plus may benefit elasticity and hydration. As you age, your body produces less collagen, leading to dry skin and the formation of wrinkles (4).

However, several studies have shown that collagen peptides or supplements containing collagen may help slow the aging of your skin by reducing wrinkles and dryness (5, 6, 7, 8).

In one study, women who took a supplement containing 2.5–5 grams of collagen for eight weeks experienced less skin dryness and a significant increase in skin elasticity compared to those who did not take the supplement (7).

Another study found that women who drank a beverage mixed with a collagen supplement daily for 12 weeks experienced increased skin hydration and a significant reduction in wrinkle depth compared to a control group (6).

The wrinkle-reducing effects of collagen supplements have been attributed to their ability to stimulate your body to produce collagen on its own (4, 5).

Additionally, taking collagen supplements may promote the production of other proteins that help structure your skin, including elastin and fibrillin (4, 5).

Summary:

Taking supplements that contain collagen may be helpful for slowing the aging of your skin. However, stronger evidence is needed from studies examining the effects of collagen on its own.

Research:

1. https://www.ncbi.nlm.nih.gov/books/NBK21582/
2. https://www.ncbi.nlm.nih.gov/pubmed/17076983
3. https://www.ncbi.nlm.nih.gov/pubmed/26362110
4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3583892/
5. https://www.researchgate.net/publication/259628887_Oral_Intake_of_Specific_Bioactive_Collagen_Peptides_Reduces_Skin_Wrinkles_and_Increases_Dermal_Matrix_Synthesis
6. http://www.jmnn.org/article.asp?issn=2278-1870;year=2015;volume=4;issue=1;spage=47;epage=53;aulast=Borumand
7. https://www.ncbi.nlm.nih.gov/pubmed/23949208
8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4206255/

2. Helps Relieve Joint Pain

Collagen helps maintain the integrity of your cartilage, which is the rubber-like tissue that protects your joints.

As the amount of collagen in your body decreases as you get older, your risk of developing degenerative joint disorders such as osteoarthritis increases (9).

Some studies have shown that taking collagen supplements may help improve symptoms of osteoarthritis and reduce joint pain overall (2, 9).

In one study, 73 athletes who consumed 10 grams of collagen daily for 24 weeks experienced a significant decrease in joint pain while walking and at rest compared to a group that did not take it (10).

In another study, adults took two grams of collagen daily for 70 days. Those who took collagen had a significant reduction in joint pain and were better able to engage in physical activity than those who did not take it (11).

Researchers have theorized that supplemental collagen may accumulate in cartilage and stimulate your tissues to make collagen.They have suggested this may lead to lower inflammation, better support of your joints and reduced pain (12).

If you want to try taking a collagen supplement for its potential pain-relieving effects, studies suggest you should start with a dosage of 8–12 grams daily (9, 13).

Summary:
Taking collagen supplements has been shown to reduce inflammation and stimulate collagen synthesis in the body. This may help promote pain relief for people with joint disorders such as osteoarthritis.

Research:
(2) https://www.ncbi.nlm.nih.gov/pubmed/17076983
(9) http://www.scielo.br/pdf/rbgg/v19n1/1809-9823-rbgg-19-01-00153.pdf
(10) https://www.ncbi.nlm.nih.gov/pubmed/18416885
(11) https://www.ncbi.nlm.nih.gov/pubmed/22486722
(12) https://www.ncbi.nlm.nih.gov/pubmed/17076983
(13) https://www.ncbi.nlm.nih.gov/pubmed/11071580

3. Could Prevent Bone Loss

Your bones are made mostly of collagen, which gives them structure and helps keep them strong (14).

As collagen in your body deteriorates as you age, bone mass does too. This may lead to conditions such as osteoporosis, which is characterized by low bone density and linked with a higher risk of bone fractures (14, 15).

Studies have shown that taking collagen supplements may have certain effects in the body that help inhibit the bone breakdown that leads to osteoporosis (9, 13).

In one study, women took either a calcium supplement combined with 5 grams of collagen or a calcium supplement and no collagen daily for 12 months.
By the end of the study, the women taking the calcium and collagen supplement had significantly lower blood levels of proteins that promote bone breakdown than those taking only the calcium (16).

Another study found similar results in 66 women who took 5 grams of collagen daily for 12 months.
The women who took the collagen had an increase of up to 7% in their bone mineral density (BMD), compared to women who did not consume collagen (17).

BMD is a measure of the amount of minerals, such as calcium, in your bones. Low BMD is associated with weak bones and the development of osteoporosis (18).

Summary:
Consuming collagen supplements may help reduce the risk of bone disorders such as osteoporosis. They have the potential to help increase BMD and lower levels of proteins in the blood that stimulate bone breakdown.

Research:
(9) http://www.scielo.br/pdf/rbgg/v19n1/1809-9823-rbgg-19-01-00153.pdf
(13) https://www.ncbi.nlm.nih.gov/pubmed/11071580
(14) https://www.ncbi.nlm.nih.gov/pubmed/16341622
(15) https://www.ncbi.nlm.nih.gov/pubmed/26163201
(16) https://www.ncbi.nlm.nih.gov/pubmed/25314004
(17) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5793325/
(18) https://www.ncbi.nlm.nih.gov/pubmed/15025843

4. Could Boost Muscle Mass

Between 1–10% of muscle tissue is composed of collagen. This protein is necessary to keep your muscles strong and functioning properly (19).

Studies suggest that collagen supplements help boost muscle mass in people with sarcopenia, the loss of muscle mass that happens with age (20).

In one study, 27 frail men took 15 grams of collagen while participating in an exercise program daily for 12 weeks. Compared to men who exercised but did not take collagen, they gained significantly more muscle mass and strength (20).

Researchers have suggested that taking collagen may promote the synthesis of muscle proteins such as creatine, and may also stimulate muscle growth after exercise (20).

Summary:

Research has shown that consuming collagen supplements increased muscle growth and strength in people with age-related muscle mass loss.

Research:
(19) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177172/
(20) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4594048/

5. Promotes Heart Health

Researchers have theorized that taking collagen supplements may help reduce the risk of heart-related conditions. Collagen provides structure to your arteries, the blood vessels that carry blood from your heart to the rest of your body. Without enough collagen, arteries may become weak and fragile (1).

This may lead to atherosclerosis, a disease characterized by the narrowing of the arteries. Atherosclerosis has the potential to lead to heart attack and stroke (21).

In one study, 31 healthy adults took 16 grams of collagen daily for six months. By the end, they had experienced a significant reduction in measures of artery stiffness compared to before they started taking the supplement (22).

Additionally, they increased their levels of "good" HDL cholesterol by an average of 6%. HDL is an important factor in the risk of heart conditions, including atherosclerosis (22).

Summary:
Taking collagen supplements may help reduce the risk factors associated with heart conditions such as atherosclerosis.

Research:
https://www.ncbi.nlm.nih.gov/books/NBK21582/
(21) https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0062943/
(22) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5429168/

6. Other Health Benefits

Collagen supplements may have other health benefits, but these have not been studied extensively.

- Hair and nails: Taking collagen may increase the strength of your nails by preventing brittleness. Additionally, it may stimulate your hair and nails to grow longer (23).

- Gut health: Although there is no scientific evidence to support this claim, some health practitioners promote the use of collagen supplements to treat intestinal permeability, or leaky gut syndrome.

- Brain health: No studies have examined the role of collagen supplements in brain health. However, some people claim they improve mood and reduce symptoms of anxiety.

- Weight loss: Some believe that taking collagen supplements may promote weight loss and a faster metabolism. There have not been any studies to support these claims.

- Summary: Collagen supplements have been claimed to promote brain, heart and gut health, as well as to help control weight and keep hair and nails healthy. However, currently there's little-to-no evidence for these effects.

- (23) https://www.ncbi.nlm.nih.gov/pubmed/28786550

Foods That Contain Collagen

Collagen is found in the connective tissues of animals. Thus, foods such as chicken skin, pork skin, beef and fish are sources of collagen (8, 24, 25).

Foods that contain gelatin, such as bone broth, also provide collagen. Gelatin is a protein substance derived from collagen after it has been cooked (24).

More research is needed to determine if eating collagen-rich foods actually helps increase collagen in your body. There have not been any human studies on whether collagen-rich foods have the same benefits as supplements.

Collagen in food is broken down into individual amino acids and peptides by digestive enzymes.

The collagen in supplements has already been broken down, or hydrolyzed, which is why it is thought to be absorbed more efficiently than the collagen in foods.

Summary:
Several foods contain collagen, including animal foods and bone broth. However, their absorption is not as efficient as that of hydrolyzed collagen.

Research:
(8) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4206255/
(24) https://www.ncbi.nlm.nih.gov/pubmed/25884286
(25) https://www.ncbi.nlm.nih.gov/pubmed/24852756

Collagen Side Effects
Currently, there are not many known risks to taking collagen supplements.

However, some supplements are made from common food allergens, such as fish, shellfish and eggs. People with allergies to these foods should avoid collagen supplements made with these ingredients to prevent allergic reactions.
Some people have also reported that collagen supplements leave a lingering bad taste in the mouth (13).

Additionally, collagen supplements have the potential to cause digestive side effects such as feelings of fullness and heartburn (13).

Regardless, these supplements appear to be safe for most people.

Summary:
Collagen supplements may lead to side effects such as a bad taste in the mouth, heartburn and fullness. If you have allergies, make sure to purchase supplements that aren't made from collagen sources you're allergic to.

III) Hyaluranic Acid

Hyaluronic acid, also known as hyaluronan, is a clear, gooey substance that is naturally produced by your body. The largest amounts of it are found in your skin, connective tissue and eyes.

Its main function is to retain water to keep your tissues well lubricated and moist. Hyaluronic acid has a variety of uses. Many people take it as a supplement, but it's also used in topical serums, eye drops and injections.

Here are 7 scientifically backed benefits of taking hyaluronic acid.

1. Preserve Bone Strength
New animal research has begun to investigate the effects of hyaluronic acid supplements on bone health.

Two studies have found that hyaluronic acid supplements can help slow the rate of bone loss in rats with osteopenia, the beginning stage of bone loss that precedes osteoporosis (40, 41).

Test-tube studies have also shown that high doses of hyaluronic acid can increase the activity of osteoblasts, the cells responsible for building new bone tissue (42, 43).

While its effects on human bone health have not yet been studied, early animal and test-tube studies are promising.

Summary:
Animal and test-tube research suggests that high doses of hyaluronic acid may help prevent bone loss, but no research has been conducted in humans.

Research:
(40) https://www.ncbi.nlm.nih.gov/pubmed/15573687
(41) https://www.ncbi.nlm.nih.gov/pubmed/23256527
(42) https://www.ncbi.nlm.nih.gov/pubmed/12926041
(43) https://www.ncbi.nlm.nih.gov/pubmed/14555276

2. Relieve Joint Pain by Keeping Bones Well Lubricated
Hyaluronic acid is also found in the joints, where it keeps the space between your bones well lubricated (22).

When the joints are lubricated, the bones are less likely to grind against each other and cause uncomfortable pain.

Hyaluronic acid supplements are very helpful for people suffering from osteoarthritis, a type of degenerative joint disease caused by wear and tear on the joints over time.

Taking 80–200 mg daily for at least two months has been shown to significantly reduce knee pain in people with osteoarthritis, especially those between the ages of 40 and 70 years old (23, 24, 25, 26).

Hyaluronic acid can also be injected directly into the joints for pain relief. However, an analysis of over 12,000 adults found only a modest reduction in pain and a greater risk of adverse effects (27).

Some research shows that pairing oral hyaluronic acid supplements with injections can help extend pain-relieving benefits and increase the amount of time between shots (28).

Summary:
Hyaluronic acid supplements are effective at reducing joint pain in people with osteoarthritis. Injections can also be used but may come with risks.

Research:
(22) https://www.ncbi.nlm.nih.gov/pubmed/17091377
(23) https://www.ncbi.nlm.nih.gov/pubmed/23226979/
(24) https://www.ncbi.nlm.nih.gov/pubmed/18208600
(25) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4729158/
(26) https://www.ncbi.nlm.nih.gov/pubmed/25415767
(27) https://www.ncbi.nlm.nih.gov/pubmed/22868835
(28) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5814393/

3. Promotes Healthier, More Supple Skin
Hyaluronic acid supplements can help your skin look and feel more supple. Roughly half of the hyaluronic acid in your body is present in your skin, where it binds to water to help retain moisture (1).

However, the natural aging process and exposure to things like ultraviolet radiation from the sun, tobacco smoke and pollution can decrease its amounts in the skin (2, 3).

Taking hyaluronic acid supplements may prevent this decline by giving your body extra amounts to incorporate into the skin (4, 5).

Doses of 120–240 mg per day for at least one month have been shown to significantly increase skin moisture and reduce dry skin in adults (3).

Hydrated skin also reduces the appearance of wrinkles, which may explain why several studies show that supplementing with it can make skin appear smoother (6, 7).

When applied to the surface of the skin, hyaluronic acid serums can reduce wrinkles, redness and dermatitis (8, 9, 10).

Some dermatologists even inject hyaluronic acid fillers to keep skin looking firm and youthful (11, 12).

Summary:
Hyaluronic acid supplements can help increase skin moisture and reduce the appearance of fine lines and wrinkles. Topical treatments can soothe redness and dermatitis, while injections can make skin appear firmer.

Research:
(1) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3583886/
(2) https://www.ncbi.nlm.nih.gov/pubmed/19808648
(3) https://www.ncbi.nlm.nih.gov/pubmed/25014997
(4) https://www.ncbi.nlm.nih.gov/pubmed/18959406
(5) https://www.ncbi.nlm.nih.gov/pubmed/18391466
(6) https://www.ncbi.nlm.nih.gov/pubmed/22956862
(7) https://www.ncbi.nlm.nih.gov/pubmed/28761365
(8) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3970829/
(9) https://www.ncbi.nlm.nih.gov/pubmed/22052267
(10) https://www.ncbi.nlm.nih.gov/pubmed/21896129
(11)https://www.ncbi.nlm.nih.gov/pubmed/10642054
(12) https://www.ncbi.nlm.nih.gov/pubmed/18384619

4. Can Speed Wound Healing
Hyaluronic acid also plays a key role in wound healing. It's naturally present in the skin, but its concentrations increase when there is damage in need of repair.

Hyaluronic acid helps wounds heal faster by regulating inflammation levels and signaling the body to build more blood vessels in the damaged area (13, 14).

Applying it to skin wounds has been shown to reduce the size of wounds and decrease pain faster than a placebo or no treatment at all (15, 16, 17, 18).

Hyaluronic acid also has antibacterial properties, so it can help reduce the risk of infection when applied directly to open wounds (19, 20).

What's more, it's effective at combating gum disease, speeding up healing after tooth surgery and eliminating ulcers when used topically in the mouth (21).

While the research on hyaluronic acid serums and gels is promising, there has been no research to determine whether hyaluronic acid supplements can provide the same benefits. However, since oral supplements boost the levels of hyaluronic acid found in the skin, it's reasonable to suspect they may provide some benefit.

Summary:
Applying hyaluronic acid directly to an open wound can help speed up the recovery process. It's unknown whether supplementing with it would have the same effect.

Research:
(13) https://www.ncbi.nlm.nih.gov/pubmed/26978861
(14) https://www.ncbi.nlm.nih.gov/pubmed/25039417
(15) https://www.ncbi.nlm.nih.gov/pubmed/22399081
(16) https://www.ncbi.nlm.nih.gov/pubmed/25115285
(17) https://www.ncbi.nlm.nih.gov/pubmed/22405094
(18) https://www.ncbi.nlm.nih.gov/pubmed/24848975
(19) https://www.ncbi.nlm.nih.gov/pubmed/10328647
(20) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5423572/
(21) https://www.ncbi.nlm.nih.gov/pubmed/27280412

5. Soothe Acid Reflux Symptoms
New research shows hyaluronic acid supplements may help reduce symptoms of acid reflux. When acid reflux occurs, the contents of the stomach are regurgitated up into the throat, causing pain and damage to the lining of the esophagus. Hyaluronic acid may help soothe the damaged lining of the esophagus and speed up the recovery process.

One test-tube study found that applying a mixture of hyaluronic acid and chondroitin sulfate to acid-damaged throat tissue helped it heal much faster than when no treatment was used (29).

Human studies have also shown benefits. One study found that taking a hyaluronic acid and chondroitin sulfate supplement along with an acid-reducing medication decreased reflux symptoms 60% more than taking acid-reducing medication alone (30).

A second study showed that the same type of supplement was five times more effective at reducing acid reflux symptoms than a placebo (31).

Summary:
A combination supplement containing hyaluronic acid and chondroitin sulfate may help reduce the symptoms of acid reflux in some people.

Research:
(29) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3387832/
(30) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5347926/
(31) https://www.ncbi.nlm.nih.gov/pubmed/24379055

6. Relieve Dry Eye and Discomfort
Approximately 1 out of 7 older adults suffer from symptoms of dry eye due to reduced tear production or tears evaporating too quickly (32).

Since hyaluronic acid is excellent at retaining moisture, it's often used to treat dry eye. Eye drops containing 0.2–0.4% hyaluronic acid have been shown to reduce dry eye symptoms and improve eye health (33, 34, 35).

Contact lenses that contain slow-release hyaluronic acid are also being developed as a possible treatment for dry eye (36, 37).

In addition, hyaluronic acid eye drops are frequently used during eye surgery to reduce inflammation and speed wound healing (38, 39).

While applying them directly to the eyes has been shown to reduce dry eye symptoms and improve overall eye health, it is unclear whether oral supplements

have the same effects. To date, no studies have examined the effects of hyaluronic acid supplements on dry eye, but it may be a future area of research.

Summary:
Hyaluronic acid is naturally found in the eyes and often an ingredient in eye drops to relieve dry eye symptoms. It's unknown whether supplementing with it would have the same effects.

Research:
(32) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3306104/
(33) https://www.ncbi.nlm.nih.gov/pubmed/11584850
(34) https://www.ncbi.nlm.nih.gov/pubmed/26783978
(35) https://www.ncbi.nlm.nih.gov/pubmed/19034126
(36) https://www.ncbi.nlm.nih.gov/pubmed/19156504
(37) https://www.ncbi.nlm.nih.gov/pubmed/26176811
(38) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1772195/
(39) https://www.ncbi.nlm.nih.gov/pubmed/17502996

7. Could Prevent Bladder Pain
Approximately 3–6% of women suffer from a condition called interstitial cystitis, or painful bladder syndrome (44).

This disorder causes abdominal pain and tenderness, along with a strong and frequent urge to urinate (45).

While the causes of interstitial cystitis are unknown, hyaluronic acid has been found to help relieve the pain and urinary frequency associated with this condition when inserted directly into the bladder through a catheter (46, 47, 48).

It's unclear why hyaluronic acid helps relieve these symptoms, but researchers hypothesize that it helps repair damage to bladder tissue, making it less sensitive to pain (49, 50).

Studies have not yet determined whether oral hyaluronic acid supplements can increase amounts of it in the bladder enough to have the same effects.

Summary:

Hyaluronic acid can relieve bladder pain when inserted directly into the bladder through a catheter, but taking supplements by mouth may not have the same effects.

Research:
(44) https://www.ncbi.nlm.nih.gov/pubmed/25623737
(45) https://www.ncbi.nlm.nih.gov/pubmed/25155120
(46) https://www.ncbi.nlm.nih.gov/pubmed/16032779
(47) https://www.ncbi.nlm.nih.gov/pubmed/24636240
(48) https://www.ncbi.nlm.nih.gov/pubmed/27627755
(49) https://www.ncbi.nlm.nih.gov/pubmed/17462486
(50) https://www.ncbi.nlm.nih.gov/pubmed/17784979

Possible Side Effects and Precautions
Hyaluronic acid is generally very safe to use, with few reported side effects. Since the body naturally produces it, allergic reactions are very rare.

One study in 60 people with osteoarthritis who took 200 mg daily for one year reported no negative side effects (23).

However, its effects during pregnancy or breastfeeding have not been thoroughly studied, so these groups should be cautious and avoid supplementing with it. There is also some evidence that cancer cells are sensitive to hyaluronic acid and taking supplements could make them grow faster (51, 52).

For this reason, it is generally advised that people with cancer or a history of cancer avoid supplementing with it (53).

Hyaluronic acid injections into the skin or joints have a higher risk of side effects. However, negative reactions are mostly associated with the injection procedure, rather than hyaluronic acid itself (54, 55).

Summary:
Hyaluronic acid is generally very safe when used as a supplement, but people who are pregnant or have cancer or a history of cancer may want to avoid taking it.

Research:
(23) https://www.ncbi.nlm.nih.gov/pubmed/23226979/

(51) https://www.ncbi.nlm.nih.gov/pubmed/18564137
(52) https://www.ncbi.nlm.nih.gov/pubmed/18661346
(53) https://www.ncbi.nlm.nih.gov/pubmed/26410544
(54) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2890129/
(55) https://www.ncbi.nlm.nih.gov/pubmed/10945374

The Bottom Line
Hyaluronic acid supplements can be safely taken by most people and provide many health benefits.

Hyaluronic acid is well known for its skin benefits, especially alleviating dry skin, reducing the appearance of fine lines and wrinkles and speeding up wound healing. It can also help relieve joint pain in people with osteoarthritis.

Other notable applications include hyaluronic acid eye drops to relieve dry eye and inserting hyaluronic acid directly into the bladder via catheter to reduce pain.

Overall, hyaluronic acid is a beneficial supplement for a variety of conditions, especially those related to skin and joint health.

IV) MSM (Methyl Sulphonyl Methane)

MSM is a chemical in animals, humans, and many plants. People use it most often to try to treat arthritis.

Why do people take MSM?
People take MSM mostly using it to lessen inflammation.

They take MSM to try to relieve pain or swelling from:
- Osteoarthritis or rheumatoid arthritis
- Bursitis, tendinitis, or tenosynovitis
- Osteoporosis
- Muscle cramps
- Scleroderma

Temporomandibular joint (TMJ) disorders
Headaches or hangover
Premenstrual syndrome
Inflammation in eyes or mucous membranes

People also apply MSM to the skin to try to treat problems such as:
Scar tissue or stretch marks
Wrinkles
Wind or sun burn
Wounds, cuts, or abrasions

Or they may take it to try to treat gastrointestinal problems such as:
Chronic constipation
Ulcers
Diverticulosis (a bowel disease)

There is evidence that MSM may help a bit with the pain and swelling of knee osteoarthritis. Also, early animal research shows some promise for decreasing joint degeneration.

Limited small studies also show that MSM may help with exercise recovery. But researchers have more work to do to confirm this.

MSM has shown some effectiveness for treating allergies, repetitive stress injuries, certain bladder disorders like intestinal cystitis, and wounds.

What dosage should be used?
People usually take from 500 milligrams of MSM three times daily to 3 grams twice daily for osteoarthritis. However, optimal doses of MSM have not been set for any condition. And quality and active ingredients in supplements may vary widely from maker to maker. This makes it hard to set a standard dose.

Can you get MSM naturally from foods?
Very small amounts of MSM can be found in fruit, corn, tomatoes, tea and coffee, and milk. But the amounts in these foods are a small fraction of the amount in supplements.

What are the risks of taking MSM?

So far studies have shown minimal side effects when MSM is taken orally, but some people may experience mild gastrointestinal side effects such as discomfort or diarrhea.
There doesn't appear to be an interaction between MSM and medications, herbs, supplements, or foods.

V) Acerola Extract

Acerola is a fruit. It is rich in vitamin C, and also contains vitamin A, thiamine, riboflavin, and niacin.

Acerola is used to treat or prevent scurvy, a disease caused by vitamin C deficiency. Acerola is also used for preventing heart disease, “hardening of the arteries” (atherosclerosis), blood clots, and cancer.

Some people use it to treat the common cold, pressure sores, bleeding in the eye (retinal hemorrhages), tooth decay, gum infections, depression, hay fever, and collagen disorders. Athletes use acerola for improving physical endurance.

How does it work?
The health benefits of acerola are due to its vitamin C content.

Scientific names: Malpighia glabra, M. emarginata, M. punicifolia
Common names: Acerola also is known as Barbados cherry, West Indian cherry, Puerto Rican cherry, Antilles cherry, cereso, cereza, cerisier, and semeruco.

his small shrub or tree has 5-petaled flowers ranging from pink to white in color. Acerola fruit is a bright red cherry-like fruit containing several small seeds. Mature fruits are soft and pleasant tasting. They contain 80 percent juice. The fruits deteriorate rapidly once removed from the tree.

Acerola is believed to originate from the yucatan. Traditionally, the fruits have been used to treat dysentery, diarrhea, and liver disorders. Other ethnobotanical uses include as an astringent and for fever.

Vitamin supplementation

Both species of *Malpighia* have been reported to be excellent sources of vitamin C. However, the fruit of *M. emarginata* is known more accurately as acerola and is one of the richest sources of vitamin C.

Acerola is used as a source of food and juice. Because of its high concentration of vitamin C, it also is sold as a natural health supplement.

Acerola provides other useful vitamins and minerals. Acerola contains from 1 to 4.5 percent vitamin C (1,000 to 4,500 mg/100 g) in the edible portion of the fruit. This far exceeds the content of vitamin C in peeled oranges (about 0.05 or 50 mg/ 100 g).

The content of vitamin C in acerola varies with ripeness (highest in green and lowest in fully ripened fruit). It also varies with the season and climate. Vitamin C analysis regarding acerola storage finds freezing the fruits to be the best way to preserve vitamin C, as compared with room temperature or refrigeration.

In addition, acerola contains vitamin A (4,300 to 12,500 IU/100 g) at about the same level as in carrots.

Other constituents include thiamine, riboflavin, niacin, calcium, iron, and bioflavonoids. It also contains phosphorus, malic acid, pantothenic acid, potassium, and magnesium. The sugars dextrose, fructose, and sucrose are also present. Acerola analysis in another report finds protein, fiber, lipids, and fatty acids. Zinc and other minerals are present, as well.

Vitamin C is an essential coenzyme that is required for normal metabolic function.

There is a potential advantage to using acerola as a source of vitamin C. The advantage is that one receives not only ascorbic acid but also several other useful vitamins and minerals from the fruit. Whether this is superior to the use of a multiple vitamin preparation has not been determined.

Antioxidant

Vitamin C is known to strengthen the immune system and build collagen cells. It also supports the respiratory system. Vitamin C is known to be an effective antioxidant. The antioxidative qualities of acerola make it an ideal ingredient in skin care products to fight cellular aging. In another report, acerola extract was shown to enhance the antioxidant activity of soy and alfalfa extracts, acting synergistically. This may be beneficial in coronary artery disease.

VI) Curcumine C3 complex®

Information taken from http://www.sabinsa.com/products-from-sabinsa/127-curcumin-c3-complex

Turmeric, derives its name from the Latin term *terra merita*, meaning 'meritorious earth', referring to the color of ground turmeric, which resembles a mineral pigment. In many languages, turmeric is named simply as 'yellow root'.

Turmeric is one of the most popular traditionally used herb and also known as "**golden spice**". According to Sanskrit medical treatises and Ayurvedic and Unani systems, turmeric has been used as traditional medicine in the treatment of various diseases like asthma, cough, allergic conditions, jaundice, diarrhea, biliary disorders, anorexia, diabetic wounds, sprains and swellings caused by injury.

Traditional Uses of Turmeric

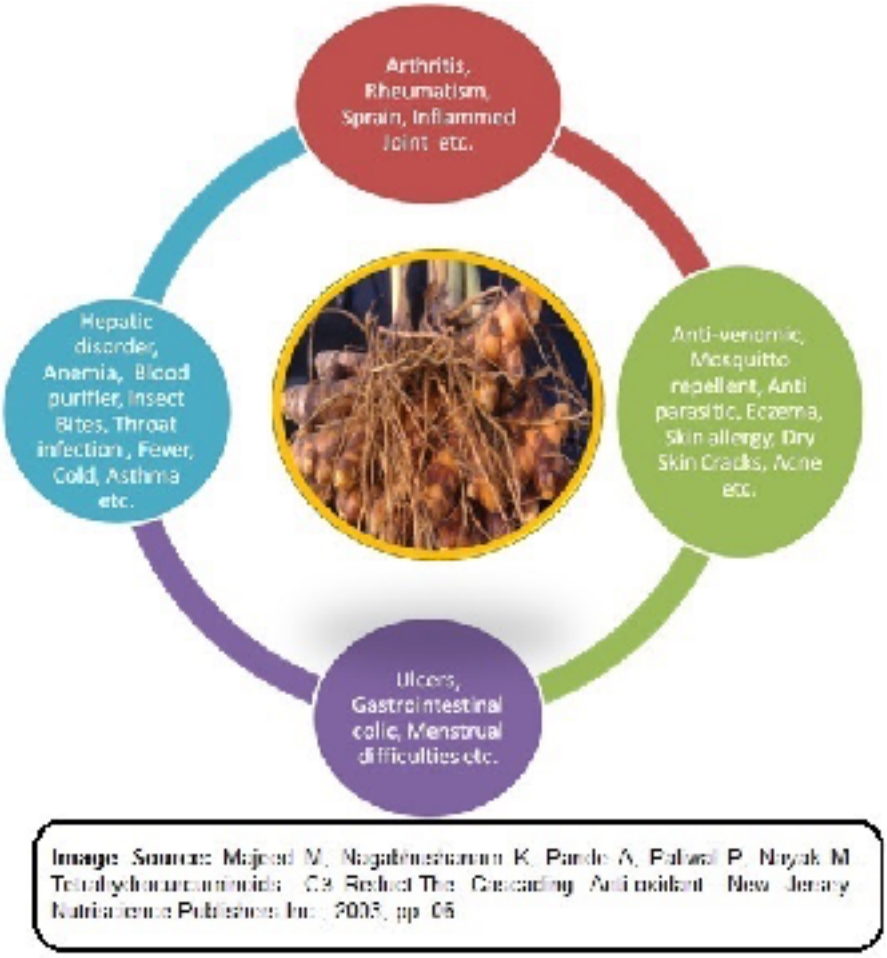


Image Source: Majeed M, Nagabhushanam K, Pandey A, Pahwa P, Nityak M Tetrahydrocurcuminoids: C3 Reduced The Cascading Anti-oxidant New Jersey Nutriscience Publishers Inc; 2005. pp 05

Genesis of Curcumin C3 Complex®

Turmeric is grown in various parts of India and other Asian countries and has been held sacred since ancient times. The use of turmeric dates back nearly 4000 years to the Vedic culture in India, where it was used as a culinary spice and had some religious significance where people regarded it as “herb of the sun”.

It probably reached China by 700 AD, East Africa by 800 AD, West Africa by 1200 AD, and Jamaica in the eighteenth century. In 1280, Marco Polo—an Italian merchant traveller described this spice “marveling” at a vegetable that exhibited qualities so similar to that of saffron.

Turmeric is one of the most revered plants. Though originated in the Indian subcontinent, but today it is used worldwide as a health food supplement, spice, natural food colorant and even as a cosmetic ingredient.

Much of the credit for the popularity of turmeric goes to the ancient texts of Ayurveda written almost 2500 years ago, describing the benefits of turmeric. However, it is modern science which has made it possible for millions to get the health benefits from turmeric's unique compounds.

Ayurveda practiced in India for ages used turmeric in several traditional formulations and was provided as personalized treatment by practitioners, however, it encountered a major hurdle while using these formulations in the Western world due to lack of the concept of standardization. Hence, standardization of herbal formulations is essential in order to assess the quality of medicines based on the concentration of actives.

Stepping Stones: Bridging Ancient Knowledge with Modern Science

- The "concept of standardization" was realized by the researchers at Sami/ Sabinsa in very early days of their work on turmeric. Sabinsa for the first time introduced this modern science concept for actives in the turmeric extracts to bring the best out of Ayurveda

- This concept of bio-standardization was later used in several herbal products by the industry as a standard tool

- The scientific team at Sabinsa Corporation derived an optimized composition of Curcuminoids from rhizomes of turmeric to provide maximum antioxidant or bioprotectant activity

- Later this unique and patented composition of Curcuminoids was marketed under the brand name **"Curcumin C3 Complex®"**—available as a dietary supplement/ nutraceutical/ functional food/ health food

- Curcumin C3 Complex® achieved a major landmark in 2013 when it received "**No Question" GRAS affirmation from the USFDA**, which meant that it achieved the Generally Recognized as Safe (GRAS) status and now could be used in the food category as well

- There are more than 80 research papers including 45+ clinical studies that have been published in peer-reviewed journals and counting..!

- Today, Curcumin C3 Complex® enjoys the special status of being the **"Most Extensively Studied and Clinically Documented"**

The journey of Curcumin C3 Complex® clinical trials has helped exploring the potential of Curcumin in preventive healthcare and has carved a unique place for Curcumin in the dietary supplement industry making it "The Most Trusted Brand" for over two decades.

Reference: Aggarwal BB, Nagabhushanam K, Pande A, Vaidyanathan P, Nayak M, Bani S, *et al*. Modulation of Immune System by Curcumin. In: Majeed M and Majeed A (Eds.), Curry Powder to Clinical Significance, 1st edition, New Jersey, NutriScience Publishers, LLC. 2015; pp.67.

The Detailed Cultivation Practices:

In India, it is reported that turmeric is grown in an area of approximately 194,000 hectares with an annual rhizome production of around 892,000 tons. The main turmeric growing states are Andhra Pradesh, Assam, Karnataka, Kerala, Maharashtra, Orissa and Tamil Nadu. Erode (Tamil Nadu) and Sangli (Maharashtra) are the major producers and trading centers of turmeric in Asia. Indian turmeric is considered the best in the world market because of its high Curcumin content.

Turmeric can be grown in diverse tropical conditions from sea level to 1500m above sea level, at a temperature range of 20-35 oC with an annual rainfall of 1500 mm or more, under rain-fed or irrigated conditions. Though it can be grown on different types of soils, it thrives best in well-drained sandy or clay loam soils with a pH range of 4.5-7.5 with good organic status.

The land is prepared with the receipt of early monsoon showers. The soil is brought to a fine tilth by giving about four deep ploughings. Hydrated lime (500 kg/ha) has to be applied for laterite soils and thoroughly ploughed. Immediately with the receipt of pre-monsoon showers, beds of 1.0 m width, 15 cm height and of convenient length are prepared with spacing of 50 cm between beds. Planting is also done by forming ridges and furrows.

Whole or split mother and finger rhizomes are used for planting and well developed healthy and disease-free rhizomes are to be selected. Small pits are made with a hand hoe on the beds with a spacing of 25 cm x 30 cm. Pits are filled with well decomposed cattle manure or compost, seed rhizomes are placed over it then covered with soil. The optimum spacing in furrows and ridges is 45-60 cm

between the rows and 25 cm between the plants. A seed rate of 2,500 kg of rhizomes is required for planting one hectare of turmeric.

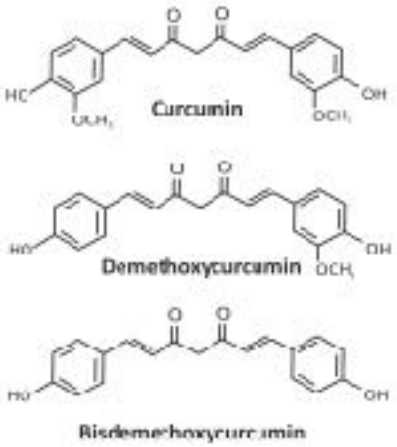
Farmyard manure (FYM) or compost at 30-40 t/ha is applied by broadcasting and ploughed at the time of preparation of land or as basal dressing by spreading over the beds or in to the pits at the time of planting. Fertilizers at 60 kg N, 50 kg P2O5 and 120 kg K2O per hectare are to be applied in split doses. Zinc at 5 kg/ha may also be applied at the time of planting and organic manures like oil cakes can also be applied at 2 t/ha. In such case, the dosage of FYM can be reduced. Integrated application of coir compost (at 2.5 t/ha) combined with FYM, biofertilizer (Azospirillum) and half recommended dose of Nitrogen, Phosphorous and Potassium (NPK) is also recommended.

Weeding has to be done thrice at 60, 90 and 120 days after 4 turmeric planting depending upon weed intensity. In the case of irrigated crop, depending upon the weather and soil conditions, about 15 to 23 irrigations are to be given in clayey soils and 40 irrigations in sandy loams.

Turmeric can be grown as an intercrop in coconut and areca nut plantations.

Harvesting:
Depending upon the variety, the crop becomes ready for harvest in 7-9 months after planting during January-March. Early varieties mature in 7-8 months, medium varieties in 8-9 months and late varieties after 9 months.

The land is ploughed and the rhizomes are gathered by hand picking or the clumps are carefully lifted with a spade. The harvested rhizomes are cleared of mud and other extraneous matter adhering to them.



Sabinsa's Curcumin C3 Complex® is obtained from the dried rhizomes of *Curcuma longa* (Turmeric) and standardized for minimum 95% Curcuminoids. The name C3 Complex® has reference to its three main chemical compounds - Curcumin, Demethoxycurcumin (DMC) and Bisdemethoxycurcumin (BDMC)— **collectively known as "Curcuminoids".**

Curcumin C3 Complex®		
Curcumin	BDMC Bisdemethoxycurcumin	DMC Demethoxycurcumin

Curcumin C3 Complex® is a patented and clinically evaluated **"Bioprotectant"** composition of three Curcuminoids.

Reference: *Molecules* 2014.DOI:10.3390/molecules191220091

Physico-chemical Properties:

- Curcumin is a yellowish crystalline, odorless powder (melting point 184-186°C), poorly soluble in water, petroleum ether and benzene; soluble in ethyl alcohol, glacial acetic acid and in propylene glycol; very soluble in acetone and ethyl ether.

- Absorption spectra of Curcumin and Curcuminoids are very similar, with their maximum absorption (λ) at 429 nm and 424 nm, respectively.

- Below table displays physico-chemical analysis of turmeric powder.

Reference: Majeed M, Nagabhushanam K, Pande A, Paliwal P, Nayak M. Tetrahydrocurcuminoids: C3 Reduct® - The Cascading Anti-oxidant. New Jersey: Nutriscience Publishers, LLC., 2012; pp.09.

Curcumin: Structural Characteristics:

- Curcumin, a symmetric molecule, is also known as **diferuloyl methane.**

- **Chemical formula:** C21H20O6 and **Molecular weight:** 368.38.

- Three chemical entities are in the structure: **Two aromatic ring systems** containing o-methoxy phenolic groups, connected by a seven carbon linker consisting of an α, β-unsaturated β-diketone moiety.

- Exists in multiple tautomeric states in which the diketone is stable in the enol state while being **easily deprotonated to the keto state.**

Classification of Active Compounds in Turmeric:

The active compounds in turmeric are typically classified as non-volatile or volatile compounds:

- Major non-volatile compounds are Curcuminoids, mainly Curcumin, Demethoxycurcumin and Bisdemethoxycurcumin.

- Major volatile compounds identified are ar-turmerone, α-turmerone, β-turmerone (curlone), ar-curcumene, zingiberene, α-phellandrene, 1, 8-cineol and some other sesquiterpenes. Turmerones are sesquiterpenoid cyclic ketones, accounting for 40-50% of the volatile oil.

The Curcuminoids:

The rhizomes of turmeric abound in many phenolic compounds known as Curcuminoids —responsible for the yellow color. It is comprised of Curcumin (75–81%), Demethoxycurcumin (15–19%) and Bisdemethoxycurcumin (2.5–6.5%).

Most of commercial Curcuminoids sold as "Curcumin", are mixtures of the three Curcuminoids. Curcumin C3 Complex®, the branded composition of natural Curcuminoids, pioneered and patented by Sabinsa Corporation, is a well characterized composition.

The Curcumin C3 Complex® is standardized to contain ≥95% Curcuminoids by HPLC analysis and is currently being used by several clinical researchers with Investigational New Drug (IND) approval from the USFDA and other regulatory organizations overseas.

Pleiotropic effects and polypharmacology:

In modern medicine, the first Curcumin study on human diseases was reported in 1937 by Oppenheimer. Since then Curcumin has been noted in more than 4,000 reports on the wide spectrum of biological activities from antioxidant to anti-inflammatory to anticancer.

These effects known as ***"pleiotropic effects"*** are highly dependent on ability of the molecule to interact and regulate multiple targets.

Hence, Curcumin, which has the ability to interact with several molecular targets, represents the term **"*polypharmacology*"** as a classical example that elucidates the concept of "one drug-multiple targets" rather than traditional concept of "one drug-one target".

Curcumin exhibits its biological activities by direct binding and indirect modulation (upregulation or downregulation) of targets. These biological activities are influenced by its chemical structure—two phenyl groups connected by a methylene bridge that allows different conformations.

Such flexible chemical structure bring about ability to Curcumin to modulate or interfere several biochemical pathways— a versatility towards broad-spectrum of targets.

Various molecular targets of curcumin include inflammatory molecules, enzymes, growth factors, transcription factors, kinases, receptors and metal ions.

Analysis of Chemical Structure *vis-a-vis* Biological Activity:

- As previously mentioned, through covalent and non-covalent interactions Curcumin exhibits modulating effects on a wide number of protein molecules either indirectly or directly

- Studies using molecular modeling and docking—biophysical tools have shown that curcumin as well as its analogs directly interact with various target proteins such as inflammatory molecules, enzymes, carrier proteins and nucleic acids, for example tumor necrosis factor-α, cyclooxygenase-1 and 2 etc

- Curcumin and its anmargin-bottom:15px;logs bindings to most of these proteins at very low concentrations (Binding constant has been detected in the nM-μM range)

As discussed earlier, because of its inherent chemical functionality—can exhibit several different conformations—directly binds to diverse proteins with high affinity. The moieties such as phenyl, hydroxyl, methoxyl and the 1,3-dicarbonyl functional groups offer a strong and directed electrostatic interaction helping enhanced favourable binding-free energies.

Furthermore, Curcumin displays additional chemical functionality as it undergoes the "keto-enol tautomerism" as a result of the β-diketone moiety. It has been observed that enol form— the predominant form allows the midsection of the molecule to act as both hydrogen bond donor and acceptor; it may also act as a chelator for positively charged metals present in the active sites of target proteins.

Reference: Majeed M. and Badmaev V. Curcuminoids-Pharmacological Actions Including Pre-Clinical and Clinical Evaluations. In: Curcuminoids: Antioxidant phytonutrients, New Jersey, Nutriscience Publishers Inc., 2003;pp. 32.

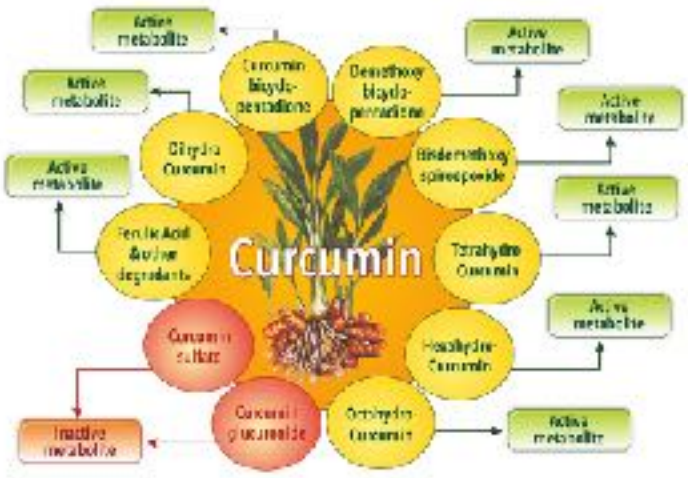
Pharmacokinetics:

Curcumin possesses tremendous potential to benefit human health; however, its rapid biotransformation has often been cited as a reason for its limited bioavailability.

Initial studies carried out to understand its pharmacokinetic properties indicated that following oral administration, Curcumin showed poor absorption resulting in lower blood concentration (traces) and most of it getting excreted in the faeces.

Since Curcumin undergoes rapid biotransformation in the gut and liver, it leads to speculations regarding the bioavailability and metabolic fate of Curcumin. As the research on Curcumin progressed with time, today we have a better insight of Curcumin's metabolism in the body.

Curcumin is metabolized by both conjugation and reduction pathways in the body resulting in formation of several metabolites.



Reference: Aggarwal BB, Nagabhushanam K, Pande A, Vaidyanathan P, Nayak M, Bani S, et al. Modulation of Immune System by Curcumin. In: Majeed M and Majeed A (Eds.), Curry Powder to Clinical Significance, 1st edition, New Jersey, NutriScience Publishers, LLC. 2015; pp.159.

1) Potentiating Therapeutic Utility of Curcumin C3 Complex® with BioPerine®:

- Conjugates like glucuronides and sulphates were found to be pharmacologically inactive

- Recent studies on tetrahydrocurcuminoids (THCs)—reduced metabolites provided interesting comparison with Curcuminoids in biological activity (antioxidant, anti–inflammatory, antidiabetic, antihyperlipidemic, antiglycation, neuroprotective and hepatoprotective activities)

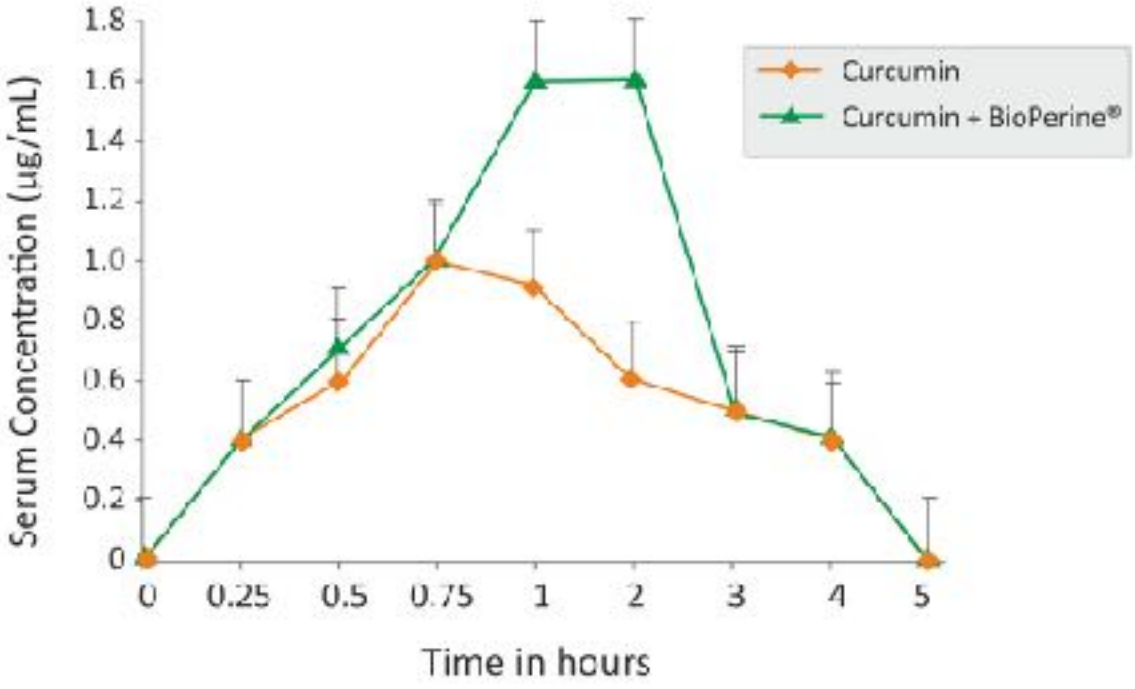
- In 2011, Proceeding of National Academy of Sciences (PNAS) published a report that Curcumin was able to generate THCs by undergoing enzymatic reduction through an enzyme-CurA, present in commensal gut microbes *E. coli*—a path breaking observation (Reference: *PNAS*. 2011;108(16):6615–20)

- Scientists at Sabinsa discovered the natural solution to improve biological activity of Curcumin in the form of BioPerine®

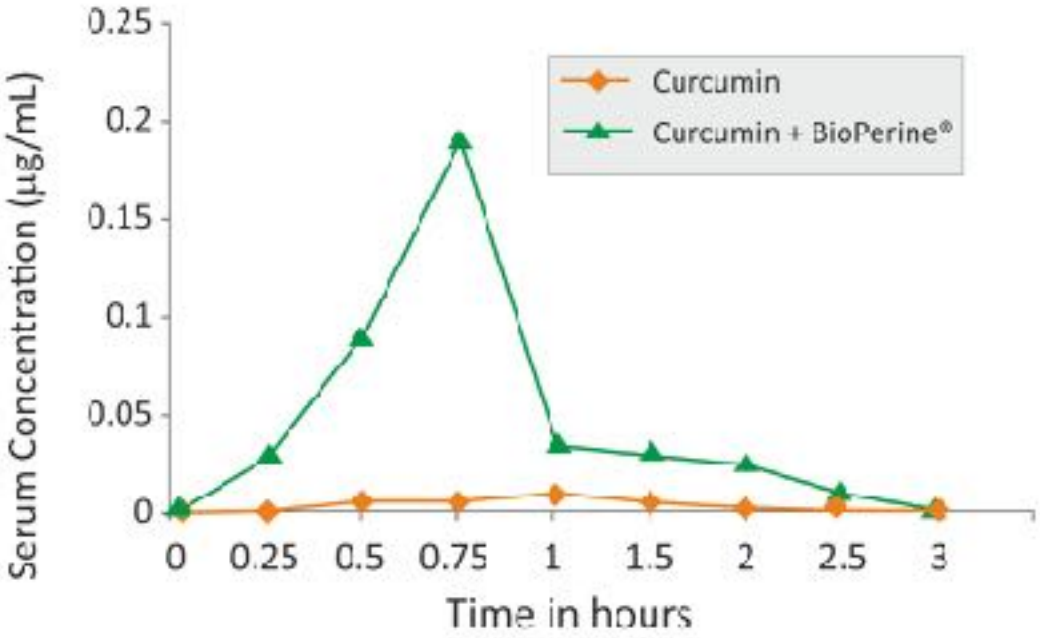
- BioPerine® is the extract standardized to 95% piperine, obtained from black pepper fruits (*Piper nigrum*) — well known for its thermogenic activity and is an inhibitor of hepatic and intestinal glucuronidation

- Sabinsa evaluated the bioavailability of Curcumin C3 Complex® in presence of BioPerine® (a patented product of Sabinsa) both preclinical and clinical

Influence of Piperine on the Pharmacokinetics of Curcumin Preclinical Study Findings:



- For the study, albino wistar rats (n=96) of both sexes were selected
- Animals were divided into two groups: one group received Curcumin (2 g/kg) alone, whereas second group was given Curcumin (2 g/kg) followed by BioPerine® (20 mg/kg)
- Pharmacokinetic profile was determined for both groups at different intervals: 0, 0.25, 0.50, 0.75, 1, 2, 3, 4, 5 & 6 h
- Results clearly showed the presence of Curcuminoids in higher concentration in the serum at 1 h and 2 h of administration of the combination of Curcumin and BioPerine®
- These encouraging results led to carry out the clinical trial for this combination



Clinical Study Findings:

- Shobha *et al.* carried out a randomized, cross-over clinical study at St. John's Medical College, Bangalore, India to assess the potential of BioPerine® for increasing the bioavailability of Curcuminoids

- Ten healthy volunteers aged between 20–26 years were enrolled in this study

- The subjects were administered 2 g Curcumin followed by two weeks of washout period and crossed-over to receive 2 g of Curcumin and BioPerine® (20 mg) combination

- Blood samples were taken at 0.25, 0.5, 0.75, 1, 2, 3, 4, 5 and 6 h post administration on each occasion

- The outcome results were in accordance with earlier performed preclinical study

- Results demonstrated that BioPerine® enhanced the oral bioavailability of Curcumin with Curcumin serum concentration peaking at 1 h and relative bioavailability of Curcumin was found to be increased by 2000% or 20 folds by BioPerine®

- Both Curcumin and Curcumin-BioPerine® combination were well tolerated by the subjects with no adverse events

This study was path-breaking and first of its kind to demonstrate bio-enhancing potential of piperine in BioPerine®. The evidence showed that piperine is a potent inhibitor for metabolism of certain nutrients/dietary ingredients, which can alter the rate of glucuronidation in gut and liver, thus slowing down the transformation and increasing bioavailability of the nutrients.

Reference: *Shoba et al*. Influence of Piperine on the Pharmacokinetics of Curcumin in Animals and Human Volunteers. *Planta Med*.1998;64(4):353–56.

Most degenerative diseases are driven by chronic, sub-clinical inflammation. The old view of the inflammation is that it represents the healing process. This is true to a certain extent; however when the inflammation becomes chronic, it becomes a disease.

Today the study of inflammation has gone from the tissue levels deeper into the nuclear level. Cell-signaling molecules have been identified which stimulate the gene that induce the expression of the COX enzyme, which in turn induce inflammation.

Nuclear Factor-κB: The Master Regulator of Inflammation
Nuclear Factor-Kappa B (NF-κB), as the 'master switch', is the primary means by which inflammation is 'adjusted'.

http://www.entrechem.com/en/development/index.html

- In the normal state NF-κB resides in the cytoplasm of the cell and is bound to its inhibitor—IkB (Inhibitor of κB)

- Injuries and inflammatory stimuli, such as free radicals trigger the release NF- κB from IkB

- The free NF-κB, now moves into the nucleus and activates the genes responsible for expressing cyclooxygenase-2 (COX-2)

- **This leads to inflammation. Inflammation plays a major role in development of most diseases.**

NF-κB activation is a major mediator of inflammation in most diseases and inhibition of NF-κB can help prevent/delay the onset of the disease.
Curcuminoids—natural compounds derived from turmeric roots, inhibit NF-κB.

2) In vitro assessment of the combined effect of eicosapentaenoic acid, green tea extract and curcumin C3 on protein loss in C2C12 myotubes
***In Vitro Cell Dev Biol Anim.* 2016; DOI 10.1007/s11626-016-0051-z**

Cachexia, a progressive wasting syndrome, which involves loss of both adipose tissue and skeletal muscle, which eventually leads to the death of the patient, has been witnessed in at least 50% of all cancer patients.

Catabolic effect of cytokines (e.g. tumour necrosis factor-α, TNF-α) and tumor products (e.g. proteolysis-inducing factor, PIF) are considered to be majorly responsible weight loss, although anorexia is initially experienced by such patients.

Hence, in addition to nutritional support, it is necessary to include an anti-catabolic agent, such as Eicosapentaenoic acid (EPA).

Eicosapentaenoic acid is a fish oil constituent known to attenuate the catabolic effect of TNF-α and PIF as well as increased protein degradation in cachexia, both *in vitro* and *in vivo*. Several clinical trials have also suggested the beneficial role of EPA in different types of cancer.

However, with higher cost, poor patient compliance and limited sources of fish oil, alternative methods of increasing the activity of EPA are viable. Hence, the current study was carried out to assess the effect of EPA, when combined with Curcumin and green tea extract (GTE), the other two known anti-catabolic agents *in vitro* experimental models.

Objective:
To investigate whether curcumin or GTE enhances the effect of low dose EPA in attenuating the depression of protein synthesis and protein degradation in C2C12 murine myotubes.

Study Design:

Measurement of total protein degradation, protein synthesis and diameter was done in C2C12 myotubes in the presence or absence of PIF and TNF-α.

Results and Discussion:

- Synergistic potential of combination of a low dose of EPA (having minimal anti-cachectic activity) with curcumin or GTE on TNF-α- and PIF-mediated protein synthesis and degradation was determined in C2C12 myotubes

- Individually, EPA (50 μM) or curcumin (10 μg/ml) did not show significant effect on PIF-induced protein degradation, however the combination produced complete inhibition ($p<0.05$)

- Similarly, for TNF-α, combination of EPA with Curcumin showed better attenuation of protein degradation ($p<0.05$) than EPA alone

- Although EPA completely attenuated TNF-α-induced depression of protein synthesis, but not that caused by PIF, whereas the combination of EPA with curcumin significantly enhanced protein synthesis to both agents ($p<0.05$)

- A significant decrease in the diameter of myotube (23.5% for TNF-α and 11.8% for PIF) was observed. However, the triple combination of EPA, curcumin and GTE returned diameters to values as that of control (both $p<0.01$)

- Researchers suggested that anti-catabolic effect of EPA (at low effective concentrations) was enhanced by curcumin and GTE by attenuating protein degradation as well as protein synthesis degradation induced by both PIF and TNF-α

Conclusion:
Overall, it was suggested that the combination of curcumin or GTE, or both with EPA enhanced its anti-catabolic effect, thus could be of utility in attenuating muscle loss in cancer patients with cachexia.

3) Curcumin: a double hit on malignant mesothelioma.
Cancer Prev Res. 2014;7(3):330-40

Malignant mesothelioma is an asbestos-related malignancy with a dismal prognosis and poor therapeutic strategies. Malignant mesothelioma originates from the mesothelial cells that line the pleural cavity, pericardium and peritoneum.

Patients have the poor median survival rate at 9–12 months from time of diagnosis and therapeutic interventions are limited to chemotherapy, surgery, radiation, immunotherapy, targeted molecular therapy and gene therapy.

Hence, there is an urgent need for effective compounds as incidence and mortality of malignant mesothelioma in less developed countries with economically disadvantaged populations is on the rise.

Although Curcumin has been identified as a potential candidate in various cancer types, little research has explored its role in malignant mesothelioma.

Objective:
To evaluate the cytotoxic effects of Curcumin in malignant mesothelioma cell killing via induction of pyroptosis and reactive oxygen species (ROS) production.

Study Design:
Various cells were evaluated for cell viability, total RNA, Caspase-1 activity, proteins like high mobility group box 1 (HMGB1), and inflammatory mediators like IL-1β, IL-18 and ROS.

Results:

- A significant inhibition of growth of malignant mesothelioma cells when treated with Curcumin doses of 40 and 50 μM for 48 and 72 h

- Malignant mesothelioma cells treated with Curcumin resulted in significantly increased extracellular (secreted) levels of HMGB1, a marker of cell death, analyzed as a parameter to support the occurrence of pyroptosis

- Curcumin showed significant cytotoxicity in HMESO cells through pyroptosis

- Treatment of HMESO cells with Curcumin (40 μM for 48 h) resulted in significantly ($p \leq 0.05$) reduced levels of inflammasome-related gene expression involved in inflammation, NF-κB, toll like receptors (TLR) and IL-1 pathways

Conclusion:
Cytotoxic effect induced by Curcumin on malignant mesothelioma cells was through pyroptosis and demonstrated anti-inflammatory effects as well. Hence, these results suggest that curcumin can be investigated further as a therapeutic agent in malignant mesothelioma.

4) Curcumin enhances the cytotoxic and chemo-sensitizing effects of lenalidomide in human multiple myeloma cells.
***J Hematol Malig* 2013; 3(2):1-7**

Only 80% of patients with **myeloma** respond to cytotoxic drugs and immunomodulatory drugs (IMiDs)-based therapy, which includes drugs like thalidomide, lenalidomide, bortezomib and pomalidomide.

Curcumin has been known to display a wide range of biological activities, including anti-oxidant, anti-inflammatory and cytotoxicity to numerous cancer cell types.

Objective:
To investigate the cytotoxic and chemo-sensitising effects of Curcumin alone and in combination with lenalidomide on the human myeloma cell line H929.

Study Design:
The human myeloma cell line H929 was treated with Curcumin and/or lenalidomide were cultured for 3 days before they were analysed for apoptosis. RT-PCR was done to examine the effects on certain gene expressions.

Results:
- A dose-dependent increase in cell death was observed when H929 cells were incubated with Curcumin or lenalidomide

- Combination of Curcumin (30 μM) and lenalidomide (2.5 mM) resulted in higher apoptosis compared to either Curcumin or lenalidomide alone

- Similarly, the combination suppressed cereblon gene (CRBN) mRNA expression significantly (7.7-fold)

- Multidrug resistance (MDR) genes expression was reduced post treatment with lenalidomide (2-fold), with Curcumin (4-fold), whereas combination showed 3-fold reduction

Conclusion:
Curcumin produced a cytotoxic effect additive to that of lenalidomide on H929 myeloma cells as well as enhanced the chemo-sensitizing effects of this agent.

5) Photopreventive effect and mechanism of azd4547 and Curcumin C3 Complex® on UVB-induced epidermal hyperplasia.
***Cancer Prev Res.* 2016;doi: 10.1158/1940-6207**

As indicated by the American Cancer Society, **skin cancer** is the most common of all type of cancers in the USA due to increased exposure to UV light due to ozone layer depletion. Higher risk prone individuals are those with fair complexion and sun-damaged skin.

Squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) together account for non-melanoma skin cancer (NMSC). The SCC is clinically very aggressive and undergoes metastasis, which may result in spreading of cancer around the body.

Therefore a "photo-preventive" agent is needed to prevent damage caused due to exposure to UV radiation.

In a previously published study Curcumin C3 Complex® has already shown positive effect in inhibiting UVB-induced tumor indices and multiplicity.

In current study, it has been suggested that this effect of Curcumin C3 Complex® is via the FGFR/mTOR mechanism.

Objective:
To investigate the efficacy of Curcumin C3 Complex® for protection against acute UVB induced hyper proliferation by FGFR/mTOR signaling pathway.

Study Design:
- JB6 P+ cells were exposed to UV light (290-320 nm) and lysed at given point of time for experimental analysis

- Female SKH-1 mice were pretreated with Curcumin C3 Complex® (15 mg/ kg) or vehicle (Corn oil) 5 days a week for two weeks on dorsal surface, after two weeks of acclimatization

- After two weeks of administration of intervention, mice were exposed to single dose of UVB (180 mj/cm2) radiation. After 24 hours of exposure, mice were sacrificed, blood samples were collected and plasma was isolated by centrifugation for ELISA test

- In control group, mice were pretreated with AZD4547 (5mg/kg) for two weeks and similarly exposed and processed as intervention group

- Squamous cell carcinoma cells and adjacent normal cells were derived from 21 patients diagnosed NMSC, whose sections were immunostained for FGFR2 (a fibroblast growth factor indicative of cancer) and quantified. The scores were given as: No stain =0, weak or focal staining record= 1+, moderate staining=2+ and strong staining=3+

Results and Discussion:

- Curcumin C3 Complex® was found to inhibit FGF-2-induced JB6 cell proliferation and mTOR1, mTOR2 activation

- Curcumin C3 Complex® also inhibited UVB-induced epidermal hyper proliferation and hyperplasia in mouse model and it was attenuated by FGFR inhibition

- In case of normal skin samples, the staining was weak. Tumor sections showed higher staining intensity pattern. Eight patients showed 30% of tumor and 13 patients showed 50% of tumor tissue immunostained for FGFR2

- The data of the current study suggested that pretreatment with Curcumin C3 Complex® was able to inhibit the phosphorylation of FGFR2 caused by UVB exposure

- As per the authors, this study found evidence of interaction between FGFR and mTOR signaling

Conclusion:

Curcumin C3 Complex® inhibited both mTOR and FGFR2 signaling, which can be considered as a new therapeutic strategy for advanced cancer with dual pathway dysregulations.

6) Effects of curcumin on serum cytokine concentrations in subjects with metabolic syndrome: A post - hoc analysis of a randomized controlled trial Biomed Pharmacother. 2016;82:578–82

Metabolic syndrome (MetS) is a condition associated with occurrence of hypertension, hyperglycemia, insulin resistance and low high-density lipoprotein cholesterol (HDL-C) in subjects with obesity.

In fact, obesity was proposed as principal feature associated with MetS and is also linked with a chronic low grade inflammation resulting from hypertrophied adipocytes, infiltrating macrophages and lymphocytes causing release of pro-inflammatory cytokines, which in turn generates systemic inflammation or "metabolic inflammation".

The main bioactive polyphenolic pigment of turmeric i.e. Curcumin, has shown to have anti-inflammatory, anti-oxidant and anti-tumor effects.

Curcumin has been widely studied for these activities; however limited literature is available on its effect on Mets individuals. The purpose of this post-hoc study was evaluation of effects of Curcumin C3 Complex® on the concentration of serum cytokines in MetS subjects.

Objective:
To evaluate the effect of supplementation with Curcumin C3 Complex® on concentration of serum cytokines in subjects with MetS.

Study Design:
In a randomized, double-blind, placebo-controlled, parallel-group design trial, 117 subjects who were diagnosed with MetS as per National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP-III) guidelines, were recruited by Baqiyatallah Hospital (Tehran, Iran).

The subjects were randomized for 8 weeks either to take intervention (500 mg of Curcumin C3 Complex® with 5 mg BioPerine® capsules, n=59), as a daily dose or

placebo (Lactose with 5 mg of Piperine, n=58). The blood samples were collected after overnight fasting both at the beginning and at the end of the study.

Results:

- The study results of within group analysis indicated that Curcumin C3 Complex® supplementation resulted in significant reduction in serum concentrations of TNF-α, IL-6, TGF-β and MCP-1 ($p<0.001$). In case of placebo group, serum levels of IL-6, TNF-α and MCP-1 remained unaltered, however, TGF-β was decreased ($p=0.003$).

- The results of between group analysis, showed that Intervention group (Curcumin C3 Complex® and BioPerine® had significantly greater reduction in serum concentrations of TNF-α, IL-6, TGF-β and MCP-1.

- The Curcumin C3 Complex® supplementation was found to be safe and well tolerated and no drop outs from the trial owing to any adverse effects were reported.

- The authors of the study suggested to further investigate correlation with changes in inflammatory parameters, changes in body weight and BMI as well as dose-response association of anti-inflammatory activity of Curcuminoids.

Conclusion:
The study results showed Curcumin C3 Complex® as an effective supplement for MetS subjects. Furthermore, the current study has shown that Curcumin C3 Complex® supplementation resulted in significant decrease in serum cytokine concentrations in subjects with MetS.

7) Effects of supplementation with Curcumin on serum adipokine concentrations: A randomized controlled trial
Nutrition. **2016, DOI: 10.1016/j.nut.2016.03.018**

Metabolic syndrome (MetS), also known as syndrome X, has a worldwide prevalence ranging 10-84 %. It is a bunch of several cardiometabolic risk factors, including abdominal adiposity, hyperglycemia, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C) and hypertension.

Insulin resistance and visceral adiposity are the key factors underlying MetS pathophysiology.

Owing to its proven and well established diversity of biological activities and several molecular targets, Curcumin has become an interesting phytochemical against a wide range of diseases, including MetS.

Several studies have demonstrated that Curcumin has the potential to modify almost all features of MetS, such as lowering plasma levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglyceride and glucose, and increasing those of HDL-C, and also possesses insulin-sensitizing, anti-obesity and anti-hypertensive properties.

Curcumin has also been found to be targeting adiponectin and leptin, the most studied adipokines, whose levels are suggested to be altered in patients with MetS.

Objective
To evaluate changes in serum levels of adiponectin and leptin, and the ratio of these two adipokines, following Curcumin supplementation in patients with MetS.

Study Design:

- This study was a *post-hoc* analysis performed on the samples obtained from previous investigation conducted by the same researchers' group

- The study was a 8-week, randomized, double-blind, placebo-controlled trial with a parallel group design

- Subjects were randomized to receive either Curcumin (Curcumin C3 Complex®; n = 59) or matched placebo (n =58), once they met the inclusion criteria

- Curcumin was administered at a daily dose of 1g (500 mg b.i.d.) and to improve the bioavailability of Curcumin, 5 mg piperine (BioPerine®) was also added

- Placebo capsules contained the same amount of lactose plus 5 mg piperine

- Blood samples were collected at baseline and at the end of the study, after overnight fasting

- Commercial ELISA kits were used to estimate serum concentrations of leptin and adiponectin

- Other parameters, such as weight, height, body-mass index (BMI) and systolic and diastolic blood pressures were measured according to standard procedures

Results and Discussion:

- There was a significant elevation of serum adiponectin ($p<0.001$) and a significant reduction of serum leptin concentrations ($p<0.001$) in the Curcumin supplementation group compared with placebo group

- Similarly, Curcumin supplementation resulted in significant decrease in serum leptin:adiponectin ratio in comparison to placebo group ($p<0.001$)

- Impact of Curcumin supplementation on dependent variables, such as serum lipids and glucose concentrations, and baseline differences in BMI and serum levels of glucose and HbA1c, as potential confounders of treatment response, remained significant after adjustment for changes

- Meta-analysis also suggested that Curcumin supplementation can increase adiponectin levels by 76.78% ($p=0.0330$) and reduce leptin by 26.49% ($p=0.238$)

Conclusion:
Curcumin improved serum levels of adiponectin and leptin, and leptin:adiponectin ratio in patients with MetS, which has encouraged to conduct further detailed studies to ascertain the impact of Curcumin supplementation.

8) Mitigation of Systemic Oxidative Stress by Curcuminoids in Osteoarthritis: Results of a Randomized Controlled Trial
***J Diet Suppl.* 2016;13(2):209-20.**

Osteoarthritis (OA) is a degenerative joint disease and is the most common type of arthritis. In OA the protective cartilage at the end of the bone wears away with time. This causes bones under the cartilage to rub together. The friction causes pain, swelling and loss of motion of the joint. Over the time, the joint may also lose its normal shape.

People with joint injury are also at risk of developing OA. Ongoing researches have shown that obesity could lead to OA of knee.

Pathophysiology of OA is no more only “mechanical stress” but has gone beyond in the last decade of research. In the recent times, biochemical alterations such as oxidative stress, characterized by increased formation of reactive oxygen species (ROS) and the insufficiency of biological defense mechanisms to detoxify these species have come up as key contributors in etiopathogenesis of OA.

It has been found that overproduction of ROS in the joint tissue causes several structural damages to biological membranes and extracellular matrix proteins.

Additionally, degradation of cartilage matrix results due to release of matrix metalloproteinases (MMPs) such as collagenases, gelatinases and stromelysins.

In numerous earlier studies on OA patients, elevated levels of pro-oxidant species and altered levels of antioxidants have been reported in plasma and synovial fluid.

Current treatment for OA is limited to use of analgesic and non-steroidal anti-inflammatory drugs (NSAIDs). The use of turmeric in Asian traditional medicine as a treatment of joint pain and inflammation has suggested its role in the treatment of OA. Curcuminoids being the active moiety of turmeric can be useful in managing OA.

Objective:
To evaluate the efficacy of Curcumin supplementation in reducing the oxidative stress by measuring the levels of serum concentration of important biomarkers in patients with knee OA.

Study Design:
In this randomized, double-blind, placebo-controlled, parallel-group, 6-week trial 53 subjects who complied with inclusion criteria were included in the trial and were divided in two groups. Subjects were administered either 3 capsules of Curcumin C3 Complex® formulation (500 mg Curcumin C3 Complex® and 5 mg BioPerine® combination) daily or matching placebo.

The primary efficacy measures of this trial were changes in clinical symptoms of OA using Osteo-arthritic index such as LPFI, WOMAC, VAS and improvement in stiffness, pain and increase in mobility of the joints. The biomarkers for oxidative

stress (as a secondary efficacy measure) were evaluated in both Curcumin and placebo groups.

Results:

- Out of 53, 40 subjects (Curcumin C3 Complex®; n=19 and placebo; n=21) completed the 6-week duration of study and were included in the final analysis.

- The primary outcome of the clinical study showed the improvement in the Osteo-arthritic index such as LPFI, WOMAC, VAS and improvement in stiffness, pain and increase in mobility of the joints in patients treated with Curcumin C3 Complex®- BioPerine® group.

- Serum samples evaluation demonstrated that oxidative stress was reduced significantly with increase in serum levels of SOD (superoxide dismutase) and glutathione s-transferase (GSH) and concurrently there was decrease in the malondialdehyde (MDA) concentration in Curcumin C3 Complex®- BioPerine® group

Conclusion:

Findings of the present study clearly indicated that following 6 weeks of supplementation with Curcumin C3 Complex®- BioPerine®, a significant improvement in systemic oxidative stress biomarkers was seen, which further validates antioxidant effects of Curcuminoids in chronic disease like OA.

The Safest and The Most Versatile Phytonutrient:

Curcumin C3 Complex®, Sabinsa's branded and patented product has received—**Generally Recognized As Safe (GRAS) status** after a comprehensive review of safety and toxicology data by an independent panel of scientists with international reputation. Curcumin C3 Complex® is the only Curcumin in the market that has been reviewed and acknowledged by the **USFDA** for its GRAS status.

Excerpts from USFDA's GRAS Notification on Curcumin C3 Complex®

- Curcumin C3 Complex® is intended for use as a flavoring agent (flavor enhancer) and as an antioxidant in various food categories, such as baked goods, soups, snack foods, imitation dairy products and seasonings & flavours

- An independent panel of recognized experts, qualified by their scientific training and relevant national and international experience to evaluate the safety of food and food ingredients, was convened to determine the safety of Curcumin C3 Complex® used as a food ingredient to provide consumers with a source of Curcumin in their diets

- A comprehensive search of the scientific literature and critical evaluation of the pertinent data and information for safety and toxicity information on Curcumin, its oleoresin and turmeric was conducted before determining GRAS status for Curcumin C3 Complex®

- Expert Panel members have individually and collectively concluded that Curcumin C3 Complex®, meeting the required food grade specifications and is GRAS under the conditions of its intended use

- Finally, based on the information provided by Sabinsa, as well as other information available to FDA, the agency had no questions regarding Sabinsa's conclusion that curcuminoids is GRAS under the intended conditions

http://www.curcuminoids.com/index.php/traditional-knowledge

10 Proven Health Benefits of Turmeric and Curcumin:

Turmeric may be the most effective nutritional supplement in existence.
Many high quality studies show that it has major benefits for your body and brain.
Here are the top 10 evidence-based health benefits of turmeric.

1. Turmeric Contains Bioactive Compounds With Powerful Medicinal Properties

Turmeric is the spice that gives curry its yellow color. It has been used in India for thousands of years as a spice and medicinal herb. Recently, science has started to back up what the Indians have known for a long time... it really does contain compounds with medicinal properties (1).

These compounds are called curcuminoids, the most important of which is curcumin. Curcumin is the main active ingredient in turmeric. It has powerful anti-inflammatory effects and is a very strong antioxidant. However, the curcumin content of turmeric is not that high... it's around 3%, by weight (2).

Most of the studies on this herb are using turmeric extracts that contain mostly curcumin itself, with dosages usually exceeding 1 gram per day. It would be very difficult to reach these levels just using the turmeric spice in your foods.

Therefore, if you want to experience the full effects, then you need to take an extract that contains significant amounts of curcumin. Unfortunately, curcumin is poorly absorbed into the bloodstream. It helps to consume black pepper with it, which contains piperine... a natural substance that enhances the absorption of curcumin by 2000% (3).

I personally prefer to swallow a few whole peppercorns along with my curcumin supplement, in order to enhance absorption.

Curcumin is also fat soluble, so it may be a good idea to take it with a fatty meal.

Summary:
Turmeric contains curcumin, a substance with powerful anti-inflammatory and antioxidant properties. Most studies used turmeric extracts that are standardized to include large amounts of curcumin.

Research:
(1) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3633300/
(2) https://www.ncbi.nlm.nih.gov/pubmed/17044766
(3) https://www.ncbi.nlm.nih.gov/pubmed/9619120

2. Curcumin is a Natural Anti-Inflammatory Compound
Inflammation is incredibly important. It helps the body fight foreign invaders and also has a role in repairing damage. Without inflammation, pathogens like bacteria could easily take over our bodies and kill us.

Although acute (short-term) inflammation is beneficial, it can become a major problem when it is chronic (long-term) and inappropriately deployed against the body's own tissues.

It is now believed that chronic, low-level inflammation plays a major role in almost every chronic, Western disease. This includes heart disease, cancer, metabolic syndrome, Alzheimer's and various degenerative conditions (4, 5, 6).

Therefore, anything that can help fight chronic inflammation is of potential importance in preventing and even treating these diseases. It turns out that curcumin is strongly anti-inflammatory, it is so powerful that it matches the effectiveness of some anti-inflammatory drugs (7).

Curcumin actually targets multiple steps in the inflammatory pathway, at the molecular level. Curcumin blocks NF-kB, a molecule that travels into the nuclei of cells and turns on genes related to inflammation. NF-kB is believed to play a major role in many chronic diseases (8, 9).

Without getting into the gory details (inflammation is extremely complicated), the key takeaway here is that curcumin is a bioactive substance that fights inflammation at the molecular level (10, 11, 12).

In several studies, its potency has compared favorably to anti-inflammatory pharmaceutical drugs... except without the side effects (13, 14).

Summary:
Chronic inflammation is known to be a contributor to many common Western diseases. Curcumin can inhibit many molecules known to play major roles in inflammation.

Research:

(4) https://www.ncbi.nlm.nih.gov/pubmed/12490960
(5) https://www.ncbi.nlm.nih.gov/pubmed/12490959
(6) https://www.jci.org/articles/view/57132
(7) https://www.ncbi.nlm.nih.gov/pubmed/19594223
(8) http://www.jbc.org/content/270/42/24995.full
(9) https://www.ncbi.nlm.nih.gov/pubmed/17885582
(10) https://www.ncbi.nlm.nih.gov/pubmed/12676044
(11) https://www.sciencedirect.com/science/article/pii/S0304383501006553
(12) https://www.sciencedirect.com/science/article/pii/S1357272508002550
(13) https://www.ncbi.nlm.nih.gov/pubmed/10404539
(14) https://www.ncbi.nlm.nih.gov/pubmed/15489888

3. Turmeric Dramatically Increases The Antioxidant Capacity of The Body
Oxidative damage is believed to be one of the mechanisms behind aging and many diseases. It involves free radicals, highly reactive molecules with unpaired electrons. Free radicals tend to react with important organic substances, such as fatty acids, proteins or DNA. The main reason antioxidants are so beneficial, is that they protect our bodies from free radicals.

Curcumin happens to be a potent antioxidant that can neutralize free radicals due to its chemical structure (15, 16).

But curcumin also boosts the activity of the body's own antioxidant enzymes (17, 18, 19).

In that way, curcumin delivers a one-two punch against free radicals. It blocks them directly, then stimulates the body's own antioxidant mechanisms.

Summary:
Curcumin has powerful antioxidant effects. It neutralizes free radicals on its own, then stimulates the body's own antioxidant enzymes.

Research:
(15) https://www.ncbi.nlm.nih.gov/pubmed/17569207
(16) https://pubs.acs.org/doi/pdf/10.1021/ol000173t
(17) https://onlinelibrary.wiley.com/doi/abs/10.1002/jat.1517
(18) https://www.tandfonline.com/doi/abs
10.1080/02772248.2013.829061#.UyAZAfl_t8E
(19) https://www.ncbi.nlm.nih.gov/pubmed/15650394

4. Curcumin Boosts Brain-Derived Neurotrophic Factor, Linked to Improved Brain Function and a Lower Risk of Brain Diseases
Back in the day, it was believed that neurons weren't able to divide and multiply after early childhood. However, it is now known that this does happen. The neurons are capable of forming new connections, but in certain areas of the brain, they can also multiply and increase in number. One of the main drivers of this process is Brain-Derived Neurotrophic Factor (BDNF), which is a type of growth hormone that functions in the brain (20).

Many common brain disorders have been linked to decreased levels of this hormone. This includes depression and Alzheimer's disease (21, 22).

Interestingly, curcumin can increase brain levels of BDNF (23, 24).

By doing this, it may be effective at delaying or even reversing many brain diseases and age-related decreases in brain function (25).

There is also the possibility that it could help improve memory and make you smarter. Makes sense given its effects on BDNF levels, but this definitely needs to be tested in human controlled trials (26).

Summary:
Curcumin boosts levels of the brain hormone BDNF, which increases the growth of new neurons and fights various degenerative processes in the brain.

Research:
(20) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2504526/
(21) https://www.sciencedirect.com/science/article/pii/S0006322303001811
(22) https://www.sciencedirect.com/science/article/pii/0896627391902733
(23) https://www.sciencedirect.com/science/article/pii/S0006899306027144
(24) https://www.sciencedirect.com/science/article/pii/S0166432812006997
(25) http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0031211
(26) https://link.springer.com/article/10.1007%2Fs10522-013-9422-y

5. Curcumin Leads to Various Improvements That Should Lower Your Risk of Heart Disease
Heart disease is the biggest killer in the world (27). It has been studied for many decades and researchers have learned a lot about why it happens. It turns out that heart disease is incredibly complicated and there are various things that contribute to it.

Curcumin may help reverse many steps in the heart disease process (28).

Perhaps the main benefit of curcumin when it comes to heart disease, is improving the function of the endothelium, which is the lining of the blood vessels.
It is well known that endothelial dysfunction is a major driver of heart disease and involves an inability of the endothelium to regulate blood pressure, blood clotting and various other factors (29).

Several studies suggest that curcumin leads to improvements in endothelial function. One study shows that is as effective as exercise, another shows that it works as well as the drug Atorvastatin (30, 31).

But curcumin also reduces inflammation and oxidation (as discussed above), which are also important in heart disease.

In one study, 121 patients who were undergoing coronary artery bypass surgery were randomized to either placebo or 4 grams of curcumin per day, a few days before and after the surgery. The curcumin group had a 65% decreased risk of experiencing a heart attack in the hospital (32).

Summary:
Curcumin has beneficial effects on several factors known to play a role in heart disease. It improves the function of the endothelium and is a potent anti-inflammatory agent and antioxidant.

Research:
(27) http://www.who.int/en/news-room/fact-sheets/detail/the-top-10-causes-of-death
(28) https://www.ncbi.nlm.nih.gov/pubmed/19233493
(29) https://www.ncbi.nlm.nih.gov/pubmed/10543305
(30) https://www.ncbi.nlm.nih.gov/pubmed/23146777
(31) https://www.ncbi.nlm.nih.gov/pubmed/18588355
(32) https://www.ncbi.nlm.nih.gov/pubmed/22481014

6. Turmeric Can Help Prevent (And Perhaps Even Treat) Cancer
Cancer is a terrible disease, characterized by uncontrolled growth of cells.
There are many different forms of cancer, but they do have several commonalities, some of which appear to be affected by curcumin supplementation (33).

Researchers have been studying curcumin as a beneficial herb in cancer treatment. It can affect cancer growth, development and spread at the molecular level (34).

Studies have shown that it can reduce angiogenesis (growth of new blood vessels in tumors), metastasis (spread of cancer), as well as contributing to the death of cancerous cells (35).

Multiple studies have shown that curcumin can reduce the growth of cancerous cells in the laboratory and inhibit the growth of tumors in test animals (36, 37).

Whether high-dose curcumin (preferably with an absorption enhancer like pepper) can help treat cancer in humans has yet to be tested properly.

However, there is some evidence that it may help prevent cancer from occurring in the first place, especially cancers of the digestive system (like colorectal cancer). In one study in 44 men with lesions in the colon that sometimes turn cancerous, 4 grams of curcumin per day for 30 days reduced the number of lesions by 40% (38).

Maybe curcumin will be used along with conventional cancer treatment one day. It's too early to say for sure, but it looks promising and this is being intensively studied as we speak.

Summary:
Curcumin leads to several changes on the molecular level that may help prevent and perhaps even treat cancer.

Research:
(33) https://www.ncbi.nlm.nih.gov/pubmed/12680238
(34) https://www.ncbi.nlm.nih.gov/pubmed/18462866
(35) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2758121/
(36) http://cancerres.aacrjournals.org/content/59/3/597.short
(37) http://www.eurekaselect.com/70722/article
(38) http://cancerpreventionresearch.aacrjournals.org/content/4/3/354.long

7. Curcumin May be Useful in Preventing and Treating Alzheimer's Disease
Alzheimer's disease is the most common neurodegenerative disease in the world and a leading cause of dementia. Unfortunately, no good treatment is available for Alzheimer's yet.

Therefore, preventing it from showing up in the first place is of utmost importance. There may be good news on the horizon, because curcumin has been shown to cross the blood-brain barrier (39).

It is known that inflammation and oxidative damage play a role in Alzheimer's disease. As we know, curcumin has beneficial effects on both (40).

But one key feature of Alzheimer's disease is a buildup of protein tangles called Amyloid plaques. Studies show that curcumin can help clear these plaques (41).

Whether curcumin can really slow down or even reverse the progression of Alzheimer's disease needs to be studied properly.

Summary:
Curcumin can cross the blood-brain barrier and has been shown to lead to various improvements in the pathological process of Alzheimer's disease.

Research:
(39) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2781139/
(40) https://onlinelibrary.wiley.com/doi/full/10.1111/j.1755-5949.2010.00147.x
(41) https://www.ncbi.nlm.nih.gov/pubmed/16988474

8. Arthritis Patients Respond Very Well to Curcumin Supplementation
Arthritis is a common problem in Western countries. There are several different types, but most involve some sort of inflammation in the joints.

Given that curcumin is a potent anti-inflammatory, it makes sense that it could help with arthritis. Several studies show this to be true.

In a study of patients with rheumatoid arthritis, curcumin was even more effective than an anti-inflammatory drug (42).

Many other studies have looked at the effects of curcumin on arthritis and noted improvements in various symptoms (43, 44).

Summary:
Arthritis is a common disorder characterized by joint inflammation. Many studies show that curcumin can help treat symptoms of arthritis and is in some cases more effective than anti-inflammatory drugs.

Research:
(42) https://www.ncbi.nlm.nih.gov/pubmed/22407780
(43) https://www.ncbi.nlm.nih.gov/pubmed/20657536
(44) https://www.ncbi.nlm.nih.gov/pubmed/7390600

9. Studies Show That Curcumin Has Incredible Benefits Against Depression

Curcumin has shown some promise in treating depression. In a controlled trial, 60 patients were randomized into three groups (45).

One group took prozac, another group took a gram of curcumin and the third group took both prozac and curcumin. After 6 weeks, curcumin had led to improvements that were similar to prozac. The group that took both prozac and curcumin fared best.

According to this (small) study, curcumin is as effective as an antidepressant. Depression is also linked to reduced levels of brain-derived neurotrophic factor and a shrinking hippocampus, a brain area with a role in learning and memory. Curcumin boosts BNDF levels, potentially reversing some of these changes (46).

There is also some evidence that curcumin can boost the brain neurotransmitters serotonin and dopamine (47, 48).

Summary:
A study in 60 depressed patients showed that curcumin was as effective as prozac in alleviating the symptoms of depression.

Research:
(45) https://www.ncbi.nlm.nih.gov/pubmed/23832433
(46) https://www.hindawi.com/journals/tswj/2009/624894/abs/
(47) https://link.springer.com/article/10.1007/s00213-008-1300-y
(48) https://www.sciencedirect.com/science/article/pii/S0014299905006230

10. Curcumin May Help Delay Aging and Fight Age-Related Chronic Diseases
If curcumin can really help prevent heart disease, cancer and Alzheimer's... then this would have obvious benefits for longevity. For this reason, curcumin has become very popular as an anti-aging supplement (49).

But given that oxidation and inflammation are believed to play a role in aging, curcumin may have effects that go way beyond just prevention of disease (50).

Research:
(49) https://immunityageing.biomedcentral.com/articles/10.1186/1742-4933-7-1
(50) http://www.ingentaconnect.com/content/ben/cpd/2010/00000016/00000007/art00019

VII) Chondroitin Sulfate

Chondroitin is one of the most sought after joint-supporting supplements available on the market today due to how it helps rebuild cartilage naturally and boosts recovery of tissue after injury or exercise.

Commonly available in formulas containing similar and complimentary supplements like glucosamine and MSM, it's taken by many people with joint pain, osteoarthritis, and other signs of "wear and tear" due to aging.

These substances are often used together because they have similar mechanisms of lowering inflammation and treating pain — plus they're considered very safe and pose little risk for side effects.

Although not every study has shown that chondroitin is capable of helping everyone who experiences joint pain, many studies do show support for its effectiveness and also safety. It's an important structural component of cartilage and one of the key substances that allows joints to withstand pressure.

The Natural Medicines Comprehensive Database has classified chondroitin as "possibly effective" for osteoarthritis (and glucosamine as "likely effective"), and many other authorities stand behind its use for fighting joint pain naturally in place of prescriptions. (1, 2)

What Is Chondroitin?

Chondroitin is a natural substance found in the human body and a major component of cartilage, which helps build connective tissue throughout the body, including those that form joints and the gastrointestinal (GI) tract. Because it works by retaining water, it helps add lubrication and flexibility to tissue and joints.

When found in supplement form, it can either be derived naturally from the cartilage of animals (including cows, pigs or sharks) or man-made. Drinking bone broth is probably the greatest way to obtain both glucosamine and chondroitin at home.

The form of chondroitin made in laboratory settings is called chondroitin sulfate, which is a combination of chondroitin and mineral salts that help improve its absorption. (3)

Supplements containing chondroitin can go by many different names depending on the product's specific formula: chondroitin glucosamine, glucosamine sulfate and chondroitin sulfate are all names you might encounter, for example. While the terminology might seem confusing, the various forms available can mostly all be used in same way.

Chondroitin Benefits and Uses

1. Helps Treat Osteoarthritis Joint Pain

Estimates show that over 27 million adults in the U.S. live with osteoarthritis, which is the most common type of arthritis and degenerative joint disease that's characterized by the breakdown of cartilage and increased joint pain.

Chondroitin sulfate is commonly used to treat pains associated with osteoarthritis, especially forms that affect very susceptible body parts like the knees and hands.

Overall, studies have shown that use of chondroitin tends to cause modest improvements in joint pain over the course of several months, although some people experience even more benefits and more quickly — especially when combining several supplements together and making other changes like eating an arthritis diet to treat symptoms.

According to the Arthritis Foundation, on average study participants usually experience about a 10 percent improvement in painful symptoms when using chondroitin compared to placebo. The best results are usually achieved after using a product containing it for three months or more. (4)

Recently, the University of Utah's School of Medicine conducted the largest-ever clinical study investigating the effects of chondroitin and glucosamine, called "The Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT)."

According to reports released by the National Center for Complementary and Integrative Health, GAIT is the first large-scale, multicenter clinical trial in the U.S. to test the effects of the dietary supplements glucosamine hydrochloride (glucosamine) and sodium chondroitin sulfate (chondroitin sulfate) for the treatment of knee osteoarthritis. (5)

- The GAIT study compared the effects of glucosamine and chondroitin sulfate (used separately and also in combination) to effects of a placebo and also a prescription drug.

- 16 rheumatology research centers across the U.S. and over 1,500 patients participated in the study, which lasted six months.

- Patients received one of five treatments over the course of six months, including the use of glucosamine and chondroitin, celecoxib (a popular prescription drug used for managing osteoarthritis pain) or a placebo. A positive response to any treatment was defined as a 20 percent or greater reduction in pain after six months compared to the start of the study.

- Results of the GAIT study showed that for participants with moderate to severe pain, glucosamine combined with chondroitin sulfate provided statistically significant pain relief compared with the placebo — about 79 percent had a 20 percent or greater reduction in pain versus about 54 percent for placebo group.

- Chondroitin and glucosamine actually worked for more people than the prescription did — 70 percent of participants in the celecoxib group experienced pain relief compared to placebo.

- However, for participants in the mild pain subset, glucosamine and chondroitin sulfate seemed to do less to reduce their pain. These participants on average didn't experience statistically significant pain relief like those with more severe pain did.

Results from another randomized, double-blind, placebo-controlled clinical trial that appeared in Arthritis and Rheumatism tested the effects of chondroitin taken by 162 symptomatic patients with osteoarthritis of the hand.

The results showed that patients who experienced chronic hand pain and took 800 milligrams of chondroitin sulfate (CS) daily experienced on average modest pain relief, reduced morning stiffness and improvements in overall functionality within three to six months of regular use.

Researchers also found that the majority of patients experienced no adverse side effects due to chondroitin, which often can't be said of other painkilling medications that can cause adverse effects like stomach ulcers, dependence,

digestive issues, blood pressure problems and more. The researchers' conclusion was that "CS improves hand pain and function in patients with symptomatic OA of the hand and shows a good safety profile." (6)

2. **Helps with Injury and Exercise Recovery**
Even for people without osteoarthritis, there's evidence suggesting that chondroitin used with glucosamine helps preserve valuable cartilage, decreases pain, increases physical function and enhances self-care activities. (7)

It can reduce joint stress following exercise or injury by helping the body synthesize new cartilage, keeping joints flexible and controlling the body's natural inflammatory responses.

3. Improves Wound Healing and Skin Health
Chondroitin and glucosamine are also used together to help heal wounds, skin-related defects, inflammation of the skin and even in veterinary medicine.

Chondroitin can help the body produce collagen, which is essential for skin health, healing and fighting the effects of aging on the skin.

Treatments made using chondroitin and glucosamine are often used for wound dressing even for severe wounds, plus applied over scrapes, burns and lesions to keep wounds moist and promote faster recovery. (8)

Some studies have even found that in patients with burns requiring skin grafting, the use of chondroitin in treatment gels can speed up healing time and help control inflammation significantly.

How Chondroitin Works
Chondroitin is a major component of the human extracellular matrix, linking together sugar and protein molecules and serving an important role in maintaining the structural integrity of tissue.

Its primary benefit and mechanism of action is stimulating regeneration of cartilage, which is the connective tissue that cushions the ends of bones within joints.

Within chondroitin are tightly packed sulfate groups that form a barrier that can withstand compression, shock and even electrostatic charges that damage tissue.

Chondroitin is technically a form of a complex carbohydrate, giving it shock and water-absorbing capabilities and making it crucial for allowing joint/bone movement without friction. This is why the loss of chondroitin from cartilage is a major cause of osteoarthritis that degenerates joints.

It's also important for forming tissue elsewhere in the body, including the skin, GI tract and the brain.

In regard to the the brain's extracellular matrix, it helps stabilize normal brain synapses and protects the brain from injury. Following trauma to the brain, levels of chondroitin are increased rapidly to help regenerate new tissue in order to replace damaged nerve endings.

Chondroitin vs. NSAIDs

Today, chondroitin, especially when taken along with glucosamine, is a popularly prescribed alternative to nonsteroidal anti-inflammatory drugs (NSAIDs), which are prescribed or over-the-counter painkillers used for treating chronic inflammation and pain.

NSAIDs are used daily, or at least very frequently, by millions of patients who deal with chronic pain due to various health conditions. Many experience side effects as a result of using NSAIDs, such as digestive complaints, including low stomach acid, and are not able to take NSAIDs long term.

Although very few studies done over a long period of time have directly compared the effectiveness of chondroitin alone with NSAIDs, the two seem to work similarly for lowering bone or joint pain and improving functionality, although chondroitin can take a bit longer to work than NSAIDs.

NSAIDs tend to reduce pain more rapidly (normally within several weeks), but then the effects commonly wear off. At this point the benefits of chondroitin and glucosamine actually start to become much more apparent, since it takes them some time to begin reducing inflammation and stimulating cartilage production.

Chondroitin has been studied most in regard to treating osteoarthritis symptoms, but research also shows it might also help treat other concerns like digestive disorders and signs of aging on the skin too.

Chondroitin Used with Glucosamine
What is glucosamine, and how is it different than chondroitin?

Glucosamine is also a natural anti-inflammatory compound found in human cartilage and connective tissue. Technically, glucosamine is an amino sugar that the body produces and distributes wherever tissue is located. It's naturally abundant in fluids that surround joints and in supplement form is sold for the same purposes as chondroitin sulfate.

Studies have found that glucosamine has cartilage-regenerating effects and boosts the strength and flexibility of joints. Glucosamine sulfate is the form most often used today to treat joint pains and osteoarthritis, which is a combination of glucosamine and mineral salts that the body can absorb easily.

Chondroitin used with glucosamine helps lower symptoms associated with loss of collagen and cartilage, which are found in tendons, joints, ligaments, skin and the digestive tract. These conditions can include tendonitis, bursitis and so on.

In healthy people, when cartilage becomes damaged due to overuse, injury or inflammation, new cartilage is normally produced to take its place. Unfortunately, as we get older our ability to regenerate lost cartilage and repair damaged connective tissue becomes less efficient.

In both humans and animals, glucosamine and chondroitin stimulate the production of new cartilage and can also help reduce inflammation in the process.

Today, these supplements are available in tablet, capsule, powder or liquid form and can be safely consumed with most medications or other dietary supplements. To date, more research has been done in regard to glucosamine's benefits, although the two are very often combined for better results.

When taken together benefits include:

- reduced joint pain
- improvement in functionality for patients with arthritis
- improved skin health
- better digestive function
- bone healing
- faster wound healing

Chondroitin Dosage Recommendations
At this time, there isn't a daily recommended intake for chondroitin or glucosamine. The GAIT study used these supplements in the following dosages:

- Glucosamine alone: 1,500 milligrams daily, taken as 500 milligrams three times a day

- Chondroitin sulfate alone: 1,200 milligrams daily, taken as 400 milligrams three times a day. Other studies have used doses around 800 milligrams daily and still seen some results

- Glucosamine plus chondroitin sulfate combined: same doses — 1,500 milligrams and 800–1,200 milligrams daily

- All participants in the GAIT study also look an over-the-counter painkiller (acetaminophen) regardless of which treatment group they were in. Over-the-counter painkillers have been found to be safe with use of these two supplements, so participants were allowed to take up to 4,000 milligrams (500-milligram tablets) per day to control pain except for the 24 hours before pain was assessed

Glucosamine and Chondroitin Side Effects and Precautions
Although these supplements are very unlikely to cause side effects and can help control your pain naturally, they won't necessarily work for every person and therefore shouldn't take the place of your other medications unless you've discussed this with your doctor.

It seems like these supplements are most helpful when used long term and in combination with other lifestyle factors — like an anti-inflammatory diet, exercise, stretching and stress reduction.

Currently, the American College of Rheumatology does not recommend either for the initial treatment of osteoarthritis, but it does stand behind their use as safe, alternative methods for controlling pain after inflammation associated with osteoarthritis has started to decrease. (9)

For the most effectiveness, a brand of high-quality chondroitin that combines several substances together should be taken for at least three months and used in proper doses.

The good news is that these supplements are safe to take even if you've had problems with other painkillers. Studies show that using these supplements regularly for up to three years poses little risk for side effects.

How much benefit you get from taking them ultimately depends on your starting level of inflammation, the amount of joint deterioration you've experienced, your medical history and other lifestyle choices.

The Arthritis Foundation points out that these supplements likely won't work for all patients, but "for those who take these supplements and who have seen improvements with them, they should not stop taking them. They are safe for long-term use."

Key Takeaways About Chondroitin

- It's a natural substance that helps build cartilage.
- Chondroitin and glucosamine are both considered to be very safe and effective ways to lower joint pain.
- They can be used in place of NSAIDs in patients who need long-term treatment and help with pain management, including those dealing with osteoarthritis.

Research:

(1) http://naturaldatabase.therapeuticresearch.com/(X(1)S(y2posz55lyhsk2agwkfz2yi4))/home.aspx?cs=&s=ND&AspxAutoDetectCookieSupport=1
(2) http://www.webmd.com/arthritis/osteoarthritis-women-12/arthritis-supplements
(3) http://www.webmd.com/arthritis/tc/glucosamine-and-chondroitin-topic-overview
(4) https://www.arthritis.org/living-with-arthritis/treatments/natural/supplements-herbs/glucosamine-chondroitin-osteoarthritis.php
(5) https://nccih.nih.gov/research/results/gait
(6) https://onlinelibrary.wiley.com/doi/abs/10.1002/art.30574
(7) https://www.mayoclinic.org/drugs-supplements-glucosamine/art-20362874
(8) https://www.ncbi.nlm.nih.gov/pubmed/16908060
(9) https://www.rheumatology.org/Portals/0/Files/ACR%20Recommendations%20for%20the%20Use%20of%20Nonpharmacologic

%20and%20Pharmacologic%20Therapies%20in%20OA%20of%20the%20Hand,%20Hip%20and%20Knee.pdf

VIII) Conventional Ny-RICE

For the best and complete information see https://ribus.com
Nu-RICE® is a patented hypoallergenic extract from rice bran. This natural processing aid helps hydrate ingredients and create a variety of emulsification solutions to create easier and faster processing.

It replaces synthetic with organic and natural ingredient formulations.
It improves clean label solutions consumers are demanding.

IX) Natural vitamin C (Acerola Extract)

Vitamin C:

Contributes to maintain the normal function of the immune system during and after intense physical exercise

Contributes to normal collagen formation for the normal function of blood vessels

Contributes to normal collagen formation for the normal function of bones

Contributes to normal collagen formation for the normal function of cartilage

Contributes to normal collagen formation for the normal function of gums

Contributes to normal collagen formation for the normal function of skin

Contributes to normal collagen formation for the normal function of teeth

Contributes to normal energy-yielding metabolism

Contributes to normal collagen formation for the normal function of the nervous system

Contributes to normal psychological function

Contributes to normal collagen formation for the normal function of the immune system.

Contributes to the protection of cells from oxidative stress

Contributes to the reduction of tiredness and fatigue

Contributes to the regeneration of the reduced form of vitamin E

Increases iron absorption

Vitamin C Ascorbic acid *RI=100%
Vitamin C is a vitamin. Some animals can make their own vitamin C, but people must get this vitamin from food and other sources. Good sources of vitamin C are fresh fruits and vegetables, especially citrus fruits. Vitamin C can also be made in a laboratory.

Vitamin C's Role in the Body
Vitamin C, also known as ascorbic acid, is necessary for the growth, development and repair of all body tissues. It's involved in many body functions, including formation of collagen, absorption of iron, the immune system, wound healing, and the maintenance of cartilage, bones, and teeth.

Vitamin C is one of many antioxidants that can protect against damage caused by harmful molecules called free radicals, as well as toxic chemicals and pollutants like cigarette smoke. Free radicals can build up and contribute to the development of health conditions such as cancer, heart disease, and arthritis.

Vitamin C is not stored in the body (excess amounts are excreted), so overdose is not a concern. But it's still important not to exceed the safe upper limit of 2,000 milligrams a day to avoid stomach upset and diarrhea.

Water-soluble vitamins must be continuously supplied in the diet to maintain healthy levels. Eat vitamin-C-rich fruits and vegetables raw, or cook them with

minimal water so you don't lose some of the water-soluble vitamin in the cooking water.

Vitamin C is easily absorbed both in food and in pill form, and it can enhance the absorption of iron when the two are eaten together.

Deficiency of vitamin C is relatively rare, and primarily seen in malnourished adults. In extreme cases, it can lead to scurvy -- characterized by weakness, anemia, bruising, bleeding, and loose teeth.

Vitamin C is used most often for preventing and treating the common cold. Some people use it for other infections including gum disease, acne and other skin infections, bronchitis, human immunodeficiency virus (HIV) disease, stomach ulcers caused by bacteria called Helicobacter pylori, tuberculosis, dysentery (an infection of the lower intestine), and skin infections that produce boils (furunculosis). It is also used for infections of the bladder and prostate.

Some people use vitamin C for depression, thinking problems, dementia, Alzheimer's disease, physical and mental stress, fatigue, and attention deficit-hyperactivity disorder (ADHD).

Other uses include increasing the absorption of iron from foods and correcting a protein imbalance in certain newborns (tyrosinemia).

There is some thought that vitamin C might help the heart and blood vessels. It is used for hardening of the arteries, preventing clots in veins and arteries, heart attack, stroke, high blood pressure, and high cholesterol.

Vitamin C is also used for glaucoma, preventing cataracts, preventing gallbladder disease, dental cavities (caries), constipation, Lyme disease, boosting the immune system, heat stroke, hay fever, asthma, bronchitis, cystic fibrosis, infertility, diabetes, chronic fatigue syndrome (CFS), autism, collagen disorders, arthritis and bursitis, back pain and disc swelling, cancer, and osteoporosis.

Additional uses include improving physical endurance and slowing aging, as well as counteracting the side effects of cortisone and related drugs, and aiding drug withdrawal in addiction.

Sometimes, people put vitamin C on their skin to protect it against the sun, pollutants, and other environmental hazards. Vitamin C is also applied to the skin to help with damage from radiation therapy.

Vitamin C is required for the proper development and function of many parts of the body. It also plays an important role in maintaining proper immune function.

Vitamin C is one of the safest and most effective nutrients, experts say. It may not be the cure for the common cold (though it's thought to help prevent more serious complications). But the benefits of vitamin C may include protection against immune system deficiencies, cardiovascular disease, prenatal health problems, eye disease, and even skin wrinkling.

How Much Vitamin C Is Enough?

A recent study published in *Seminars in Preventive and Alternative Medicine* that looked at over 100 studies over 10 years revealed a growing list of benefits of vitamin C.

"Vitamin C has received a great deal of attention, and with good reason. Higher blood levels of vitamin C may be the ideal nutrition marker for overall health," says study researcher Mark Moyad, MD, MPH, of the University of Michigan.

"The more we study vitamin C, the better our understanding of how diverse it is in protecting our health, from cardiovascular, cancer, stroke, eye health [and] immunity to living longer." "But," Moyad notes, "the ideal dosage may be higher than the recommended dietary allowance."

Most of the studies Moyad and his colleagues examined used 500 daily milligrams of vitamin C to achieve health results. That's much higher than the RDA of 75-90 milligrams a day for adults. So unless you can eat plenty of fruits and vegetables, you may need to take a dietary supplement of vitamin C to gain all the benefits, Moyad says. He suggests taking 500 milligrams a day, in addition to eating five servings of fruits and vegetables.

"It is just not practical for most people to consume the required servings of fruits and vegetables needed on a consistent basis, whereas taking a once-daily supplement is safe, effective, and easy to do," Moyad says. He also notes that only 10% to 20% of adults get the recommended nine servings of fruits and vegetables daily.

Moyad says there is no real downside to taking a 500-milligram supplement, except that some types may irritate the stomach. That's why he recommends taking a non-acidic, buffered form of the vitamin. "The safe upper limit for vitamin C is 2,000 milligrams a day, and there is a great track record with strong evidence that taking 500 milligrams daily is safe," he says.

Still, American Dietetic Association spokeswoman Dee Sandquist, RD, suggests doing your best to work more fruits and vegetables into your diet before taking supplements. "Strive to eat nine servings of fruits and vegetables daily, because you will get a healthy dose of vitamin C along with an abundance of other vitamins, minerals, and phytochemicals that are good for disease prevention and overall health," she says.

To meet your RDA for Vitamin C, here are all the foods and beverages you'd need to consume to reach 500 milligrams (mg):
Cantaloupe, 1 cup (8 ounces): 59mg
Orange juice, 1 cup: 97mg
Broccoli, cooked, 1 cup: 74mg
Red cabbage, 1/2 cup: 40mg
Green pepper, 1/2 cup, 60mg
Red pepper, 1/2 cup, 95mg
Kiwi, 1 medium: 70mg
Tomato juice, 1 cup: 45mg.

The Health Benefits of Vitamin C
According to recent research, vitamin C may offer health benefits in these areas:

1. Stress **.** "A recent meta-analysis showed vitamin C was beneficial to individuals whose immune system was weakened due to stress -- a condition which is very common in our society," says Moyad. And, he adds, "because vitamin C is one of the nutrients sensitive to stress, and [is] the first nutrient to be depleted in alcoholics, smokers, and obese individuals, it makes it an ideal marker for overall health."

2. Colds. When it comes to the common cold, vitamin C may not be a cure. But some studies show that it may help prevent more serious complications. "There is good evidence taking vitamin C for colds and flu can reduce the risk of developing further complications, such as pneumonia and lung infections," says Moyad.

3. Stroke. Although research has been conflicting, one study in the *American Journal of Clinical Nutrition* found that those with the highest concentrations of vitamin C in their blood were associated with 42% lower stroke risk than those with the lowest concentrations. The reasons for this are not completely clear. But what is clear is that people who eat plenty of fruits and vegetables have higher blood levels of vitamin C."People who consume more fruit and vegetables will not only have higher [blood] levels of vitamin C, but higher intake of other nutrients potentially beneficial to health, such as fiber and other vitamins and minerals," study researcher Phyo K. Myint said in an email interview.

4. Skin Aging. Vitamin C affects cells on the inside and outside of the body. A study published in the *American Journal of Clinical Nutrition* examined links between nutrient intakes and skin aging in 4,025 women aged 40-74. It found that higher vitamin C intakes were associated with a lower likelihood of a wrinkled appearance, dryness of the skin, and a better skin-aging appearance.

5. Other studies have suggested that vitamin C may also:
   Improve macular degeneration.
   Reduce inflammation.
   Reduce the risk of cancer and cardiovascular disease.

https://www.healthline.com/health/food-nutrition/acerola-cherry

(from: http://www.webmd.com/vitamins-supplements/ingredientmono-1001-vitamin+C.aspx?activeIngredientId=1001&activeIngredientName=vitamin+C&source=1 and http://www.webmd.com/diet/the-benefits-of-vitamin-c)

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