

Understanding Turmeric Anti-Inflammatory effects and Its Clinical Use.

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Abstract

Background:

Turmeric (*Curcuma Longa*) one of the most widely researched rhizomatous herbaceous plant, has been effectively utilized in its native India for thousands of years. However in these last one hundredth years, Turmeric has captured the attention of western medicine for its anti-inflammatory effects with the bulk of its clinical studies having taken place since the early 70's.

Objective:

This research paper objective is to bring clinical based evidence to both practitioners and consumers as to how Turmeric really renders its anti-inflammatory effect in the body, why it's effective on inflammatory conditions and what is the best way of delivery for optimal absorption.

Methods:

Research of computerized literature was performed to identify clinical placebo-controlled trials of Turmeric (*Curcuma longa*). Databases searched were Med-Line and Cochrane Library. Double-blind, placebo controlled studies were chosen that utilized subjects with chronic inflammatory diseases especially that of the digestive system.

Results:

Turmeric Anti-Inflammatory effects were confirmed up to 85% of success throughout the various databases, after review of information from the controlled clinical studies. Research also yielded information on how to best utilize Turmeric supplements based on its absorption rate.

Conclusion:

I was able to consolidate solid scientific information based on clinical evidence to bring a better understanding as to how Turmeric supplementation must be used, and for what type of inflammatory conditions its use is most optimal.

Introduction

There is no doubt to the efficacy of Turmeric (Curcumin Longa), in its medicinal properties, especially of its anti-inflammatory use. Its use has been well documented in India through the use of Ayurveda well before any western research study had ever been done. Turmeric (Curcumin Longa) is a fairly risk free rhizomatous herbaceous perennial plant that has been used for centuries in food, Ayurvedic medicine and as a component ingredient of many other products used in the body such as coloring, liniments, cosmetics etc..

In reviewing the average herbal books however, and even some more conventional medically inclined herbal books such as in example The Physicians' Desk Reference (PDR) for Herbal Medicines, they all seem to fail to give a deeper understanding of how and why Turmeric is effective as an anti-inflammatory agent in the human body and the research behind it.

Since the early 70's, focus was placed on Turmeric's' anti-inflammatory use and many clinical studies (NYU, 2012) took place in India as well as other places such as Thailand and China. Study documentation and publishing soon caught the attention of countries such as England, France and the United States, which in turn conducted clinical studies of their own.

Much of the clinical research test done supportive the results of its anti-inflammatory properties, but at times fail to address the actual mechanism by which Turmeric yielded particular results.

Journal published materials are often reviewed by scientist, field physicians and research advocates making the conclusions of the studies on Turmeric as well-established herb which effectiveness in its anti-inflammatory effects has become a reality for many. To this effect many in the conventional medicine world, pharmaceutical world and other herbal supplementation companies have jumped on the van wagon of this 'wonder herb supplement'.

However, what about the average consumer who will most likely never take an interest in reviewing journals of medicine both conventional or complementary to establish an educated decision of how to treat their inflammatory condition appropriately with Turmeric, with the adequate dosage and if in fact Turmeric is the right herbal product to take for a particular type of inflammatory condition.

Practitioners as well as consumers often rely on direction from labels and insert. Seldom questioning the information, consumers take it and practitioners recommended or prescribe it, falling prey to many unscrupulous fabricants who may not be utilizing the best possible process for Turmeric to be actually effective, because they do not understand the basic mechanisms of action of Turmeric in the body.

There is much clinical study evidence of its anti-inflammatory effects, but minimal understanding as to how Turmeric interacts with our bodies. It will be my objective through this research paper to establish information through the analysis of the body's inflammatory process and how Turmeric works on a cellular level to achieve the anti-inflammatory response for which Turmeric is presently well known for.

Hopefully this information will give the reader a deeper understanding on how Turmeric binds with our body, thereby empowering the reader to also make an educated decision on how to best approach the purchase and use of this herb in its natural or supplemental form.

Methods

Research of computerized literature was performed to identify clinical placebo-controlled trials of Turmeric (*Curcuma longa*). Databases searched were Med-Line and Cochrane Library. Double-blind, placebo controlled studies were chosen that utilized subjects with chronic inflammatory diseases especially that of the digestive system.

There was no discrimination in the population block utilized in terms of age, sex, gender or culture. Clinical studies utilized were not only from the United States and are no older than twenty five years, these were studies published by verifiable journal publications. In addition to this computerized search, other publications were utilized to substantiate the information about the plant in terms of cultural, historical and medicinal use.

The number of controlled clinical trials chosen were narrowed down to ten, since those selected met the criteria and had clear data about the potency, dosage in relation to the use in the medical conditions outlined and the results validated the potency of Turmeric in relation to the mechanism of absorption in the body.

Main Proposed Uses of Curcumin:

- Ulcerative Colitis, Dyspepsia (Indigestion), Crohn's Disease, Gallbladder,

Additional Proposed Uses of Curcumin:

- Diabetes, High Cholesterol, Depression, Alzheimer's disease, Rheumatoid Arthritis, Osteoarthritis, Chronic Anterior Uveitis and Multiple Sclerosis.

Keywords:

Turmeric, *Curcuma Longa*, Curcumin, Clinical Trials, placebo controlled, Anti-Inflammatory Effects, Inflammatory Response. Anti-inflammatory action, anti-carcinogenic, anti-mutagenic, anti-thrombotic action, anti-microbial action, anti-viral action, anti-parasitic action and hepatic-protective action.

Discussion

In Ayurveda, a traditional natural medicinal practice of India, Turmeric (*Curcumin Longa*) known in India as Haridra, Gauri has been prescribed for ailments affecting the digestive, respiratory and urinary system via the circulatory system (Ayurveda Encyclopedia, 2005) which means that it's a substance that must be ingested in order to render effect. If we analyze what the digestive, respiratory and urinary system have in common, in relation to the circulatory system, we have to understand the different type of tissues that make up the body. In the human body there are four type of main tissues the epithelial, connective, muscle and nervous tissue.

Organs in the body most usually share a bit of all four type of tissues, however some organs are made up of more of a particular type and in the case of the digestive, respiratory and urinary system the four are made of epithelial tissue that is highly vascular (Siumed, 2007). By design, tissue needs to have vascularity in order to be supplied with the adequate nutrients, oxygen, red blood cells and white blood cells, therefore a strong and non-occlusive circulatory system is essential in order to maintain the tissue healthy and intact. It's ultimately through the circulatory system that the delivery of nutrition or supplements will help decrease the inflammatory process in the body.

In order to understand how Turmeric anti-inflammatory agents works, one must also understand the basics of the inflammatory process in the body, how Turmeric chemical properties interpolate with the bodies anti-inflammatory process, why Turmeric is recommended mostly for particular systems in the body more so than others, how does the absorption of Turmeric works in the body and ultimately how to utilize Turmeric to yield the most medicinal effect possible.

Understanding the inflammatory process in the body:

The inflammatory process of the body can be summarized as a response of the body to injury, infection or irritation; the inflammatory response can start as a result of damage or injury, exposure to bacteria, and virus, it can also be a result of the ischemia, inadequate intake of nutritional factors, toxins and exposure to extreme temperatures or radiation. The typical inflammation we know and

recognized is when we actually are able to visualize signs of redness, swelling, pain and heat in the body. However, there are other type of inflammatory process that occur internally in our bodies, this type of inflammation is often referred as the “silent inflammation” (Sears, 2007), this kind of inflammatory process occurs in the body with or without signs or symptoms perhaps for many years before they actually appear.

The inflammatory process occurring in the internal systems or organs can be caused by many factors that create impaired epithelialization such as nutritional deficiencies, inadequate circulation or oxygenation of tissues causing hypoxemia, and the frequent use of certain drugs in the body that lower the immune system such as in the case of the use of steroids as an example.

When internal inflammation in the body occur, we can utilize certain makers to measure inflammation. Measuring the level of C - reactive protein (CRP) produce and released by the liver is the most common type of blood test utilized to determine the level of inflammation, and along with the CRP there are also other indicators in the blood that indicate an increase in inflammation such as the elevated erythrocyte count and sedimentation rate, (Clyne & Olshaker, 1999). All these indicators are a result of the increase of neutrophil production in the bone marrow that are caused by the increase of cytokines proteins otherwise known as cell communicators when an inflammation occurs.

The Inflammatory response has various mediators which kick the response itself, mediators include Histamine response, Prostaglandins P GE 2, and PGI2, Bradykinin, Serotonin and Leukotrienes. In the case of Turmeric, the mediator in which its two main curcuminoids ensures its work is with the Prostaglandins and Leukotrienes in the body.

Currently there are also other indicators to this “silent inflammation”, and that is the measurement of Arachidonic acid (AA) ratio to Eicosapentanoic acid (EPA), it’s presumed that this ratio can warn a person well in advance to the development of a degenerative or chronic condition (Schacky, Fischer & Weber 1985). AA and EPA both have an essential fatty acid interaction which allows the body to signal each other in the presence of inflammation, to collaborate and help inhibit the

inflammatory process via vasodilation, especially in the muscles, liver and brain which is where most is mostly found and metabolized. These type of essential fatty acids are abundantly found in the Omega-3 fatty acids, according to The US National Institute of Health MedlinePlus (NIH, 2013) but what makes it interesting in relation to Turmeric, is that Turmeric chemical properties work in repressing Arachidonic Acid ration to decrease inflammation while aiding Eicosapentanoic acid to also decrease inflammation therefore making each curcumoids substance in Turmeric a balancing act in the control and decrease of inflammation, this very same action in Turmeric has yielded results in research to suggest that it is an effective treatment in helping the body lower inflammation and in addition it helps improve chemotherapy response in patients.

- How Turmeric composition interpolate with the bodies anti-inflammatory process:

Turmeric molecular formula of $C_{21}H_{20}O_6$ yields two main curcuminoids, Curcumin Demethoxycurcumin and Bisdemethoxycurcumin (Cayman Chem, 2010), both curcuminoids have been extensively studied in pre-clinical studies utilizing animals, and time after time. Turmeric chemical properties have yielded jaw dropping results its anti-inflammatory effects and even inhibition of certain cancerous cells.

Turmeric anti-inflammatory chemical properties come from its derivatives of the hydroxyl and phenol groups molecules, these molecules have been shown to be essential in the inhibition of prostaglandin synthetase and leukotrienes synthesis (Kohli,.; Ali.; Ansari & Raheman,2005). Prostaglandin synthetase, simply refers to the process in which the group of lipid compounds derived from the fatty acids of the Prostaglandin are catalyzed by enzymes, breaking them down to a molecular level to produce energy derived from the process itself.

Leukotrienes synthesis on the other hand, refers to the forming of complex substances deriving from the Leukotrienes which are formed in the leukocytes and other immune cells to mediate eicosanoid inflammatory substance by way of oxidation of arachidonic acid. Together the prostaglandin synthetase and leukotrienes synthesis form by far one of the most potent anti-

inflammatory process in the tissue, which is why the Turmeric chemical properties work so wonderfully in the body to reduce inflammation.

- Turmeric application to clinical studies:

In these last thirty years, Curcumin has finally been the center of actual clinical studies among different populations. PubMed has over three hundredth thirty six research clinical studies reports over these past ten years, most of them centering on the effects of Curcumin in the use of its chemical properties in relation to anti-inflammatory effects focusing on various chronic inflammatory conditions that deal with the digestive, respiratory and urinary system its progression into cancer and how Turmeric is utilized to decrease inflammation and therefore also aiding in the treatment of some cancers, (Turmeric info, 2009) most recently researchers have attributed the main components of Turmeric Curcumoids (diferuloylmethane), exhibiting the inhibition and proliferation of various types of tumor cells and in some cases producing a cytotoxic effect to these cancerous cells (Oxford Journals, 2001).

Various pharmaceutical companies have now isolated both Demethoxycurcumin and Bisdemethoxycurcumin and both are now being further studied in different types of cancerous conditions. (Cayman Chem, 2010) Bisdemethoxycurcumin has been found to act in the process of phagocytosis of macrophages and interacting with Vitamin D3 it also acts as an amyloid- β macrophages clearance which is substantial in the suppression and proliferation in cancer. In addition Demethoxycurcumin also suppresses proliferation in cancer cells by regulating the coactivator transcriptional process suppressing the pathway and inhibiting lipopolysaccharide from which cancerous cells feed from. Therefore, Turmeric disrupts cancerous chemical processes that can instigate propagation of the malignancy.

Other studies conducted by the immunology department in Boston University indicate that Turmeric has shown to slow down cellular replication of HIV in laboratory animals and is currently

under investigation in humans (Sabinsa, 2010) and may indeed play a role in the therapeutic treatment of HIV.

Another important feature of Turmeric is its effect as an antioxidant in the body. The chemical properties of Turmeric (Sabinsa, 2010) having clinical tested to prevent the buildup of free radicals responsible for injuring tissue, much of this effect acquiescent in the cardiovascular and cerebral areas.

For the purpose of formulating and meeting the objective of this research paper, to establish relevant information in regards to the cellular process of Turmeric in our bodies, and in order to be able to utilize the recommended guidelines through the analysis of the dosages in the clinical studies (as described prior in the methods section), I have limited the use of the data to that which addresses only chronic inflammatory conditions in the digestive system which is what has been treated traditionally in Ayurvedic medicine, and have not placed emphasis in the data used in relation to cases of Diabetes, High Cholesterol, Depression, Alzheimer's disease, Rheumatoid Arthritis, Osteoarthritis, Chronic Anterior Uveitis and Multiple Sclerosis, which are other conditions that currently are also treated through the use of Turmeric, in Complementary Alternative Medicine.

Conclusions

Turmeric as demonstrated in various studies through the effects of Demethoxycurcumin and Bisdemethoxycurcumin (Srivastava; Dikshit; Srimal & Dhawan, 1985), both are inhibitors of platelet aggregation, therefore maintaining the vascular system with a healthy flow and protecting humans from strokes and heart attacks. This was also a focus of a study (Mishra & Palanivelu, 2008) among populations in two different regions in India that consumed more curry than the other, not only was there a significant decrease in heart attack and strokes by 60% percent, but in addition another very important finding was that Alzheimer's disease was found to be about 79% less in the population where curry was also consumed. Since a strong circulatory system is essential in order to maintain the tissue healthy and intact as established prior, then it makes perfect sense that Turmeric not only

delivers the curcumoids to decrease inflammation, but it does this by maintaining a healthy flow in the vascular system.

In the review of the ten clinical studies utilized to formulate the information in this research paper, it was found that one of the greatest challenge in the utilization of Turmeric, was the poor absorption and solubility rate in the body. According to UCLA professor, Greg Cole higher dosage are to be utilized in the treatment of conditions (UCLA, 2008), because of the poor solubility and absorption of Turmeric curcumoids. In addition according to Anderson M.D. who conducted a 10 year study, he mentions that it's important to understand that to increase absorption of the Curcumin Longa into the body at a cellular level, there needs to be a certain way that Curcumin needs to be processed for better absorption. There are certain other ingredients (Pantry TV, 2012) that can be utilized to increase the rate of absorption in the body such as adding pepper. In addition because of the poor oral absorption in relation to serum concentration, the need to utilize higher dosages of Turmeric causes many of the participants to experience increased gastro-intestinal bowel movements and bile production, to eliminate these side effects clinical researchers have focused their attention on developing ways to increase absorption without the need to utilize high doses.

For instance in (Dulbecco &Savarino, 2013) the Journal of Gastroenterology recent findings demonstrate that there is a new lecithin formulation that enables to increase absorption 29 times higher than traditional Turmeric products, in addition a new technology called phytosome allows the Curcumins in Turmeric to become water soluble with the Phytosomes making the absorption through the bio-membranes in the body easier to reach the circulatory system.

- Turmeric use implication

Since many chronic inflammatory conditions go on for many years, even before sign and symptoms occur, often this repetitive inflammatory process or constant exposures to irritants cause permanent damage in normal cell reproduction and eventually cells molecular formation becomes damaged. The inflammatory process becomes chronic and the immune system is overwhelmed and actually starts to

work against the body, this is when cell apoptosis occur and cancerous cells are formed and multiplied in an uncontrolled cellular division process (Anto; Mukhopadhyay; Denning & Aggarwal, 2001), eventually resulting in the demise of a particular organ tissue. Therefore it's safe to assume that the utilization of Turmeric (Curcumin Longa) decreases the chronic inflammatory episodes in the digestive, system thereby potentially aiding in the prevention of cancerous cells from forming and multiplying.

The dosages of clinical trials utilized in the treatment of chronic inflammatory disease, the utilization and the most effective means of delivery of Turmeric in order to yield the most medicinal effect possible are further discussed in the conclusions and recommendations portion of this paper. Turmeric is not only an herb utilized in Ayurveda or other complementary disciplines but now has become a mainstream, well studied substance utilized in conventional medicine. Its applications are constantly being tested and its components Demethoxycurcumin and Bisdemethoxycurcumin have been isolated to the degree where each component is being tested and utilized presently in the treatment of various types of cancer, especially those of the Gastro-intestinal system.

Recommendations

In the analysis of the various clinical research studies, and with the well-established fact of its clinical results in terms of the legitimate effect in the body; the clinical use of it now becomes the focus in establishing recommendations in its use. It's valid to state that Turmeric (Curcuma Longa) is indeed most effective in its anti-inflammatory use, especially that of the Gastro Intestinal inflammations and additionally serving as an agent of cancer prevention. Its use as an additional therapeutic agent in conjunction with other cancer treatments is presently well documented. In addition, it is being used as a preventative medicine agent for optimal circulatory system health and its effects is also showing promising effects in the use of inflammatory process in Alzheimer's. For the purpose of this paper though the clinical indications and dosage, as well as contraindications have been limited to the Gastro-Intestinal (GI), Pulmonary and Urinary systems with the majority of them going to the GI system as it's

the system that has been most clinically tested in relation to the use of Turmeric, which includes the gall bladder, liver, stomach, pancreas, and intestines.

- Safety / Side Effects:

There are no real contraindications to the use of Turmeric as the Food and Drug Administration has label it under the food category and has given the approval and status of ‘Generally Recognized as Safe’ (GRAS) in the United States and approves its consumption up to 20 mg per serving (FDA, 2014). However, most recently the FDA has listed Turmeric in doses utilized for Cancer preventative model dosages of a Dietary administration of ethanolic turmeric extract in for 14 days, in percentages that surpass the usual dosage for consumption and are generally quite high, these have been found to have a hepatotoxic effect in mice and have produced coagulative necrosis in cells of liver (FDA, 2014). These results are not substantiated by any clinical research that has been done by human consumption, but warning is always granted for those patients with liver conditions or susceptible to liver conditions.

There are no side effects to the ingestion of the standard dosage of Curcumin utilized as a preventative supplement or treatment of mild inflammation. However people with gallbladder chronic problems should avoid using it more than once a day since Turmeric intake increases contractions in the gallbladder, thereby increasing bile release (Rasyid & Lelo 1999). People receiving standardized cancer treatment should consult with their physician, however in the clinical trials, subjects received up to 8 g/day for four months with no results of toxicities, (Antony; Benny & Kaimal 2007). However in these trials, subjects did not have any prior indication or history of liver problems. Long term use though is not recommended with doses higher than 10,000 mg and should be closely monitored by a health care provider.

- Dosing:

According to the Recommended Daily Intake, Dietary Reference Intake (DRI), Curcumin can be utilized 400-600 mg three times a day (NIH, 2014), it’s recommended to be taken with food to avoid gastro-intestinal distress. The 2008 issue of the journal Biochemical Pharmacology reports the safe use

of higher doses of turmeric, especially in cancer patients, but it should be closely monitor for liver toxicity. The best indication that you are taking more than what you need is if you continue having symptoms of nausea, vomit, and diarrhea. If this symptoms are present, it's recommended to lower the dosage, especially if there is no real chronic inflammatory condition going on and it's being taken as a supplement.

- Rate of absorption:

The rate of absorption is a real issue when it comes to the consumption of Turmeric, since Turmeric bio-viability is low once it enters into the digestive system. If Turmeric is taken by itself without any having gone through any special process or added ingredients to aid in the absorption, 80% of it will be secreted in feces and urine and therefore traditionally higher doses have been administered.

Currently though along with clinical studies dealing with its effects, many pharmaceutical companies or supplemental preparation companies have also been doing research of their own in formulating ways for Turmeric to be absorbed more effectively. For example, Bioperine (Sabina, 2009) which is the main component of black pepper aids in the rate of Curcumin absorption up to 80% more than without it. Utilizing black pepper by itself along with Turmeric increases the rate of absorption by 60%. Theracumin (Integrative Therapeutics, 2014), has been one Turmeric supplementation that has hit the market with great success among many Naturopathic Doctors (Trutt, 2013). The supplement itself is treated by chemically vaporizing it and chemically stabilizing the derived components, rendering the absorption rate up to 90% according to blood level test performed. There are other preparation houses that are utilizing Lecithin to increase absorption levels, according to them up to 95% rate of absorption (Healthy Source, 2012).

Some pharmaceutical companies have actually isolated the two main curcumoids in Turmeric for Scientific studies, especially in the area of Oncology. Demethoxycurcumin and Bisdemethoxycurcumin (Cayman Chem, 2010), these two components are not usually available to the

public, but are almost 100% absorbed in the system once used and therefore higher doses can be effectively utilized in clinical trials.

Summary

After copious research, I have not only learned about Turmeric (*Curcuma Longa*) more intimately, but also have a solid understanding how it should be utilized and for what type of conditions its use is most optimal. In conclusion, I have established a solid link between legitimate clinical trials results and scientific data through the explanation of how the physiology of the body and the chemical process of Turmeric work to yield its anti-inflammatory effect, giving the reader whether a clinician or a consumer, valid information based on evidence based medicine. The information presented herein, is given primarily to help make a more judicious choice and decision on the health intervention of a client utilizing Turmeric supplements. Ultimately is about bringing scientific based facts in to give a better understanding to the consumer or providers on the properties of Turmeric and its clinical effects in a more comprehensible manner.

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