Treatment of Gastroesophageal Reflux Disease (GERD)-
Efficacy of L-Ornithine & Curcumin Derivates

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Abstract-
The purpose of this review is to summarize the pertinent literature published in the present era regarding the antiulcerogenic property of Curcumin against the pathological changes in response to ulcer affectors (*Helicobacter pylori* infection, chronic ingestion of non-steroidal anti-inflammatory drugs, and exogenous substances). The gastrointestinal problems caused by different etiologies was observed to be associated with the alterations of various physiologic parameters such as reactive oxygen species, nitric oxide synthase, lipid peroxidation, and secretion of excessive gastric acid. Gastrointestinal ulcer results probably due to imbalance between the aggressive and the defensive factors. In 80% of the cases, gastric ulcer is caused primarily due to the use of non-steroidal anti-inflammatory category of drug, 10% by *H. pylori*, and about 8-10% by the intake of very spicy and fast food. Although a number of antiulcer drugs and cytoprotectants are available, all these drugs have side effects and limitations. In the recent years a widespread search has been launched to identify new antiulcer drugs from synthetic and natural resources. An Indian dietary derivative (Curcumin), a yellow pigment found in the rhizome of Curcuma longa, has been widely used for the treatment of several diseases. Epidemiologically, it was suggested that Curcumin might reduce the risk of inflammatory disorders, such as cancer and ulcer. These biological effects are attributed to its anti-inflammatory and antioxidant activities. It can, therefore, be reported from the literature that Curcumin prevents gastrointestinal-induced ulcer and can be recommended as a novel drug for GERD treatment.

Index Terms— GERD, Curcumin, L-Ornithine, L-Arginine, Phytotherapy, Right dosage, Japanese Way-UKON
No Chikara

Introduction

Digestive disorders, including gastroesophageal reflux disease (GERD), dyspepsia, peptic ulcer disease, irritable bowel disease (IBS) and inflammatory bowel disease (IBD) affect millions of people worldwide.

GERD – A Gastric Condition

GERD is defined as a collection of symptoms or tissue damage as a result of reflux of gastric contents into the esophagus.

There are many causes to the acid reflux including lifestyle, medication, diet, pregnancy, rapid weight gain, and certain medical conditions like pregnancy, diabetes and Hiatal Hernia. It is a condition when the upper part of the stomach protrudes up above the diaphragm. Weak supportive tissues and increased abdominal pressure can contribute to the condition.

GERD is very common in the Western world and can happen to anyone, irrespective of age.

Pathophysiology of GERD

GERD usually happens because the lower esophageal sphincter (LES) — the muscular valve where the esophagus joins the stomach, opens at the wrong time or does not close properly. When the stomach contents move backward into the esophagus, this is known as gastroesophageal reflux.

The esophagus becomes irritated or inflamed because of acid backing up from the stomach. The stomach produces hydrochloric acid after a meal to aid in the digestion of food. The inner lining of the stomach resists corrosion by this acid. The cells lining the stomach secrete large amounts of protective mucus. The lining of the esophagus does not share these resistant features and stomach acid can damage it.
The condition is related to the inflammation of esophagus, just behind the heart, so the term "heartburn" was coined to describe the sensation of acid, burning the esophagus.

Common Symptoms of GERD

The symptoms include epigastric pain/discomfort, nausea, pain in the chest after meals, heartburn and regurgitation.

GERD can be the first condition that may lead to various serious complications like Esophagitis and esophageal ulcers, Laryngopharyngeal reflux, bleeding in the damaged esophageal lining, strictures, swallowing problems, respiratory problems including Asthma, Barrett’s Esophagus and Cancer of the Esophagus.

Multiple challenges are associated with GERD treatment. First, the lack of symptoms does not correlate with the absence of or the healing of esophageal lesions. Second, proton pump inhibitors, the current standard of care for GERD, are ineffective for the majority of GERD patients who have non-erosive disease.

Role of Phytotherapy in the Treatment of GERD

Digestive disorders are conventionally treated with drugs and surgery, as well as psychological and behavioral therapy. Recently, alternative or complementary medicines, such as acupuncture, and phytotherapy/dietary therapy, have become increasingly popular in persons with digestive disorders, especially when conventional therapies fail to improve their symptoms.

A survey of 539 patients attending an outpatient clinic in Spain showed that nearly two-thirds (61.6%) of patients with digestive disorders had used Phytotherapy in the past year, and patients who were female, had a university education, or were diagnosed with lower GI disorders were found to be more frequent users of Phytotherapy. Moreover, approximately 80% of these users were satisfied with the results these therapies yielded.

Curcumin and Derivates – In the Treatment of GERD

GERD results when there is an acid imbalance in the stomach. When the adequate food digestion does take place the undigested food refluxes into the esophagus, causing GERD. Turmeric prevents the condition by helping the gall bladder to produce enzyme required for proper food digestion. Compounds found in the herb increase bile acids which make the food in the stomach to be fully digested.

Turmeric is traditionally used as a herbal remedy for a variety of diseases in India and China and as an over-the-counter supplement worldwide. It is a potential therapeutic qualities by having:

- anti-inflammatory effects
- antioxidant effects
- antimicrobial effects
- anticancer effects
- carminative actions

Curcumin (C₁₅H₁₀O₆), the principal Curcuminoid, a yellow pigment found in the rhizome of Curcumaloga, also known as turmeric, has been used since ancient times in China to treat various human disorders, and it is well documented for its medicinal properties in the Indian and Chinese systems of medicine. The presence of both phenolic OH and CH₂ groups in β-diketone moiety of this natural compound contributes significantly to its potent antioxidant properties. The gastro protective potentials of Curcumin protect the patients from gastric side effects of many anti-inflammatory drugs, thereby improving the quality of life for patients and decreasing the treatment costs significantly.

Pharmacology of Turmeric (Curcuma longa)

Pharmacology of turmeric is very important to be studied as it has poor bioavailability. The pharmacological parameters to be studied are:

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PHARMACOKINETICS:

Evidence from numerous literatures revealed that Curcumin has poor absorption, bio-distribution, metabolism, and bioavailability. Thus, continuous research on Curcumin found some possible ways to overcome these problems. To increase the bioavailability, longer circulation, better permeability, and resistance to metabolic processes of Curcumin several formulations have been prepared which include nanoparticles, liposomes, micelles, and phospholipid complexes.

ABSORPTION & DISTRIBUTION OF CURCUMIN:

Uptake and distribution of Curcumin in body tissues is obviously important for its biological activity. Absorption is the movement of drug from its site of administration to circulation. The drug given as watery solution is absorbed faster than when the same is given in solid form.

Naturally occurring Curcumin is not readily absorbed and it has tendency to break down in the GI system before it can be utilized. Absorption appears to be better with food. Co-supplementation with Piperine (black pepper extract) significantly increases bioavailability of Curcumin. The big problem associated with Curcumin is that, it isn’t absorbed readily as it has poor aqueous solubility. But after enhancing its water solubility it can absorb readily into the body.

Now comes the distribution of Curcumin. Once the Curcumin gain access to the blood stream its major role is to distribute to other tissues whether interstitial or intestinal fluid. Factors determining distribution:

- Binding to plasma and tissue protein
- Blood flow
- Special compartments and barriers (plasma proteins, tissue proteins)
- Diseased states, etc.

Lipophilic nature of Curcumin makes it to cross the blood -brain barrier. At high concentrations, Curcumin binds to beta amyloid protein and inhibits its self-assembly.

Metabolism of Curcumin:

Once absorbed, Curcumin is subjected to conjugations in liver and intestine to form Curcumin sulfate and Curcumin glucuronide. The very first bio-distribution study reported the metabolism of major part of Curcumin orally administered to rats. Liver was indicated as the major organ responsible for metabolism of Curcumin. Holder et al. reported that the major biliary metabolites of Curcumin are glucuronides of tetrahydroCurcumin (THC) and hexahydroCurcumin (HHC).

Metabolites of Curcumin

Excretion:

Metabolized Curcumin is generally excreted in urine as the glucuronide and sulfate conjugates. The remainder of any dose, whether absorbed or not, is likely degraded beyond detection by the time it is excreted.

There are conflicting reports regarding the excretion of Curcumin and its metabolites in human subjects. In one study, neither the parent compound nor its metabolites were detected in blood or urine of human subjects after oral dosing, but Curcumin was recovered from faeces.

Contraindications:
In addition to the therapeutic targets, Curcumin shows broad reactivity against a number of human enzymes that are linked to compound toxicity. Curcumin may increase the bleeding risk associated with antiplatelet and anticoagulant and also decrease the efficacy of certain drugs like vinblastine, ciprofloxacin and co-trimoxazole.

Since vitamin D and Curcumin work differently with the immune system, Curcumin or a combination of two may be more effective depending on individual patient. No dosage of vitamin D and Curcumin are recommended at this point. Finally by interactions with heavy metals like chromium and lead, Curcumin prevents neurotoxicity. The chronic use of Curcumin may cause liver toxicity. A phase 1 clinical trial with 25 subjects for 3 months found no toxicity from Curcumin.

**Pharmacodynamics** (mechanism of action)

Turmeric's antioxidant properties can counter the formation of the oxygen-free radicals and prevent the damage of the esophagus.

Turmeric is a powerful anti-inflammatory medicine that also may help reduce GERD symptoms; the active ingredients in turmeric are known as Curcuminoids. One study using 162 mg of Curcumin twice daily for 4 weeks showed that patients experienced significant relief from dyspepsia and irritable bowel symptoms. Improvement was noted after patients had been on the Curcumin for one week.

Curcumin inhibited inflammatory cytokines such as TNF, cyclooxygenase (COX)-2, inducible nitric oxide synthase. Curcumin not only suppresses inflammation in intestine but strengthens its lining thus help in Crohn's disease.

Curcumin has strong antioxidant action also by inhibiting the formation and propagation of free radicals that cause deterioration of neurons in many neurogenerative disorders like Parkinson disease. It also increases level of glutathione. There are many different ways Turmeric (Curcumin) works on various gastric ailments associated with GERD, with proven results. Here's to note how:

1. It has anti-ulcer property and remedies dyspepsia

The antiulcer activity of Curcumin was displayed by attenuating the different ulcerative effectors including gastric acid hypersecretion, total peroxides, myeloperoxidase activity, IL-6, and apoptotic incidence, along with its inhibitory activity for pepsin.

**Conclusion:** Curcumin and other compounds found in turmeric help in preventing as well as healing gastric ulcers.

2. It shows microbicidal action against H.pylori

Helicobacter pylori are the infective cause behind GERD. The growth of these bacteria gives rise to symptoms of acidity and heartburn.

Sarkar et. al have the ways by which turmeric offers therapeutic action in H.pylori infection and the problems encountered in implementing this therapy. Curcumin's anti-inflammatory, antioxidant, anti-microbial and anti-carcinogenic effects are responsible for it. A study in cells and animal models show that Curcumin reduces the production of inflammatory chemicals initiated by H.pylori infection such as matrix metalloproteinases and reduces the activation of genes which are toxic to cells.)

**Conclusion:** Lab studies show that Curcumin's anti-microbial action is effective in terminating growth of H. Pylori infection.

3. It can reduce stomach inflammation

Curcumin is a strong anti-inflammatory agent; it reduces the level of inflammatory mediators and also increases the production of anti-inflammatory molecules.

Animal study shows that Curcumin treatment lowers the level of inflammatory agents secreted in the stomach due to H.pylori infection.
Nuclear factor kappa B is the protein that controls inflammatory processes. Curcumin prevents activation of nuclear factor kappa B in gastric mucosa caused by H. pylori infection.

**Conclusion:** **Curcumin's anti-inflammatory action can counteract stomach inflammation occurring in GERD.**

4. It promotes antioxidant defenses

Curcumin and other Curcuminoids are strong antioxidants. They raise the level of antioxidant enzymes and scavenge free radical species that cause oxidative damage.

This antioxidant property of Curcumin contributes to its anti-ulcer activity. In animal study, Curcumin was found to reduce oxidative stress, inflammation, and gastric acid secretion, thereby exerting a protective effect against ulcer formation. **Conclusion:** **Curcumin's antioxidant property reduces the oxidative stress and tissue injury occurring in gastric ulcer.**

5. It reduces damage caused by bile acids in esophagus

GERD is characterized by reflux of stomach contents, bile acids, and low stomach pH. Exposure of cells in the food-pipe to these acidic materials gives rise to inflammation of esophagus which is known as esophagitis.

Esophageal lining cells when exposed to a low pH induces activation of inflammatory cytokines like interleukins due to activation of nuclear factor kappa B (a protein that controls inflammatory process). Curcumin inhibits the activity of nuclear factor kappa B and prevents activation of esophageal cells in response to low pH, thus reducing esophageal inflammation in GERD.

In a lab study mimicking the conditions of bile acid damaging the esophageal cells, Curcumin treatment was found to reduce the levels of an inflammatory enzyme like COX and improves antioxidant defenses.

6. Curcumin can reduce damage caused by laryngopharyngeal reflux or silent reflux when the contents of the stomach move back to the throat and cause symptoms of hoarseness, wheezing and cough. It occurs when gastric pepsin moves to the cells of the airway and causes damage, inflammation and oxidative stress.

**Conclusion:** **Curcumin's anti-inflammatory effect is found to be beneficial in treatment of laryngopharyngeal reflux or silent reflux. This is when acids flow back to the throat and cause cough and hoarseness.**

7. Curcumin protects from gastric side effects of painkillers

NSAIDs (non steroidal anti-inflammatory drugs) or painkillers do cause gastric side effects on long-term leading to acid reflux. They cause gastritis or inflammation of tissue lining the stomach wall and among severe side effects, they may also cause gastric erosion or bleeding. **Conclusion:** **Long term consumption of painkillers can give rise to acidity like symptoms and at worse stages can lead to gastric erosion, bleeding and GERD. Curcumin is found to mitigate the gastric erosions caused by painkillers.
8. Curcumin shows therapeutic potential equivalent to conventional GERD medications

A study comparing the anti-ulcer effect of Curcumin and omeprazole (a medication prescribed to reduce acidity and treat stomach ulcers) showed that Curcumin had a stronger potential of treating ulcers compared to omeprazole. Curcumin-treated ulcers by inducing angiogenesis or formation of blood vessels in the tissue lining the stomach; this prevents and promotes healing of ulcers.

(Conclusion: Curcumin’s anti-ulcer activity was found to be better than omeprazole, a medication prescribed for treatment of GERD and peptic ulcers.)

Study During Clinical Trials

Turmeric has shown to potentially protect the GI tract through its anti-inflammatory effect. Turmeric was found to effectively improve dyspeptic symptoms in patients with dyspepsia, as well as maintain remission in patients with ulcerative colitis (UC).

In particular, a randomized controlled trial (RCT) was conducted in 116 patients with dyspeptic complaints (such as abdominal pain, epigastric discomfort, flatulence or belching). The study findings indicate that after 7 days, 87% of the turmeric group experienced symptom relief from dyspepsia compared to 53% of the placebo group ($P=0.003$).

Another RCT was conducted to assess the effect of Curcumin (the main active ingredient of turmeric) in 82 patients with UC. These patients were randomly allocated to receive 1 g Curcumin twice daily in addition to sulfasalazine or mesalamine or placebo as well as sulfasalazine or mesalamine for 6 months. At the end of the study period, fewer patients in the Curcumin group experienced relapse compared to the control group (4.7% vs 20.5%, $P=0.038$).

To date, only one methodologically rigorous systematic review of the effects of turmeric (AMSTAR score = 6) was conducted. In this study, the authors reviewed the efficacy and safety of turmeric for maintenance remission in patients with UC. The findings suggest that, of 216 identified studies, only one study met the inclusion criteria, and this included study had a low risk of bias. This systematic review concluded that Curcumin was a safe and effective therapy for maintenance of remission in patients with UC, in particular when supplemented by Mesalamine or Sulfalazine.

Given the paucity of work on the therapeutic role of turmeric, it was proposed to complete a systematic review to determine the efficacy and safety of turmeric and its compounds in patients living with digestive disorders, including dyspepsia, peptic ulcer, IBS, IBD (Crohn’s disease and UC), and GERD.

Only Right Dosage of Curcumin Works

Turmeric’s stems, or rhizomes, can be dried and ground into a powder. The powder can be taken orally or used when cooking.

Unless you add turmeric to all of your recipes or drink a lot of turmeric tea, it may be difficult for you to consume enough turmeric to treat acid reflux. Organic turmeric extract supplements may be a better way to get medicinal amounts.

Turmeric when taken in right dose can help GERD patients very effectively. However, high dosage of turmeric can also trigger acidity. The recommended dosage of Curcumin extract is required in formulation with L-Ornithine and Inositol. In GERD, the balance in the electrolyte gradient of cell membranes shall be recovered which is essential for digestion. The dosage of the supplement would differ based on the formulation, hence it is best to consult a doctor before taking turmeric supplements.

L-Ornithine is a nonprotein amino acid (not used to create proteins) that is an intermediate of the urea cycle, and provision of ornithine to a cell is actually the rate limiting step of the cycle. Ornithine binds with a molecule known as carbamoyl phosphate which requires ammonia to be produced and then is converted into L-Citrulline giving off urea as a byproduct. Due to this, the conversion is one that reduces ammonia concentrations in the blood and concomitantly increases urea. L-Ornithine is important for conditions that are
characterized by an excess level of ammonia, like GERD.

14 Piperine, For Increased Absorption

One way to increase turmeric’s absorption is to consume it with Piperine. It's commonly found in black pepper. When choosing turmeric supplements, look for brands that have black pepper extract or piperine listed as an ingredient.

Avoid taking supplements on an empty stomach and close to the time of taking medicines. Consult a health practitioner before taking turmeric supplements.

CONCLUSION

In summary, Curcumin is a well-known molecule with multiple pharmacological activities that have the potential to be used to treat many gastrointestinal diseases, both functional and organic. It appears to be a very promising therapeutic compound on the basis of thousands of pre-clinical studies, but its poor bioavailability has greatly hampered more widespread clinical use.

However, the Japanese formulation of Curcumin, Ukon No Chikara, with phospholipids has allowed us to overcome this problem by markedly improving intestinal absorption compared with the traditional unformulated Curcuminoid mixtures. 16 Ukon no Chikara is purported to detoxify the liver, helps metabolize toxins, and stimulate gastric juices. It reduces inflammation and assists in increasing the body’s antioxidant capacity. It helps to keep the liver protected, reduces blood acetaldehyde levels and promises therapeutic effects on GERD. It also replenishes vital electrolytes essential to maintain energy levels.

According to clinical trials using Curcumin with limited bioavailability, we can expect to see greater therapeutic effectiveness from phospholipid-complexed Curcumin, which enables increased absorption and appropriate tissue delivery. These improved pharmacokinetic and pharmacodynamic properties are also able to significantly reduce the required dosages of Curcumin and to increase the compliance of the product. Overall, these features make Curcumin a very promising new therapeutic option for the treatment of gastrointestinal and hepatic diseases for which present therapies are largely unsatisfactory.

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In GERD For Non Stop Relief... & Control

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