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An Indian Traditional Magical Medicine: Curcuma longa

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ABSTRACT
Turmeric (Curcuma longa) it is one of the oldest medicinal plants, which has been used from ancient times. Turmeric derived from the Zingiberaceae family and curcumin is the bioactive component in the turmeric. The purpose of this review was to provide a brief summary of the medicinal and nutritional value of curcumin. Turmeric is good source of macro and micronutrients such as protein, energy, vitamin and minerals, and t is known for various medicinal properties with antioxidant activities and it is useful in conditions such as inflammation. Accordingly, there is a need for novel agents that are effective, acceptable and nontoxic to humans. Preclinical studies in experimental animals have shown that cur cumin, an active principle of the Indian spice turmeric (Curcuma longa Linn) is effective in preventing or ameliorating UC and inflammation. The recently published papers in international cite as PubMed/ Medline, Science Ctation Index and Google Scholar about turmeric were searched . Turmeric is also used forAyurvedic and various cosmetic purposes like blood purification and different types of skin products. The purpose of this review is to provide a brief overview of the plethora of research regarding the health benefits of curcumin.

Keywords: *[curcumin, turmeric, ayurvrdic, antioxidant, anti-inflammatory]*

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I. Introduction :-

Turmeric is one of the most commonly used plants in many countries especially in Asia. Its rhizome used as spice for flavouring and Colouring of the foods. It is basically an evergreen tree having leaves which are very large, a stem which is very small and its rhizomes are yellowish in colour. Any type of harm that is caused by inflammation turmeric is used to cure that ailment. It is used for the treatment of swelling caused due to injury. Turmeric belongs to class Liliopsdia, family Zingiberacaeae, Genus Curcuma while Species curcuma longa. Its powder is used for the cure of cough, anorexia, liver disorders, abdominal disorders and diabetic wounds. Pakistan is second biggest grower of turmeric, although production quantity per acre is very low. [1]

Turmeric (curcuma longa), Amla (EmblicaOfficinalisGaertn.), and the Black pepper (Piper nigrum L.)these are culinary plants and are also used for various centuries in Indian Ayurvedic Medicine system. Turmeric use as home medicines for illness and also used for various treatment include the Unani, Siddha and Ayurveda. It is a food component used as a spice in many parts of the world. It has treatment for inflammation, fungal infection, mutagenesis, carcinogenesis, Hepatotoxicity, sterility, fibrosis, cholesterol, diabetes, ulcer, hypertension, and coagulation Problem. Now days it is used against Alzheimer's,
Rheumatoid arthritis, bowel disease, Multiple Sclerosis, HIV and Cataract. [2]

Fig 1. Turmeric

The advantages of curcumin include its cost effective, safety and easy of extraction. It was first known for its role as a food additive or spice in cooking. Turmeric is widely used as a spice, cooking additives, medicine, spices, dyes and Cosmetics; one of the important herbs..Curcumin is a natural anti-inflammatory drug. Turmeric can reduce the joint inflammation.

The usage of the turmeric plant for medical purposes dates back over 4,000 years. Turmeric is utilised in Southeast Asia both as a primary spice and as a part of religious rituals. Turmeric, which is a vivid yellow colour, is also referred to as "Indian saffron" because of this. The more than 3000 publications on turmeric that have been published in the last 25 years show that modern medicine has started to recognise its significance. The safety and effectiveness of turmeric are further discussed after discussing in vitro research, animal studies, and ultimately studies conducted on humans.[03]

For instance, turmeric, which contains the anti-inflammatory compound curcumin, has been used in curries in India, cosmetics in Thailand, beverages in China, antiseptics in Malaysia, and anti-inflammatory drugs in Pakistan. In the United States, it is also used as a preservative and colouring agent in mustard sauce, cheese, butter, and chips, as well as in capsules and powder for supplements. There are numerous ways to buy curcumin, including in the form of capsules, tablets, ointments, energy drinks, soaps, and cosmetics. Good tolerance and safety profiles have been observed, and the US Food and Drug Administration (FDA) has recognised them as "Generally Recognized as Safe." even at doses between 4000 and 8000 mg/day [04] and of doses up to 12,000 mg/day of 95% concentration of three curcuminoids: curcumin, bisdemethoxycurcumin, and demethoxycurcumin [05].Turmeric its most active compound, curcumin, has numerous scientifically proven health benefits, including the ability to improve heart health and prevent Alzheimer's and cancer. It's a potent antiinflammatory.[06]

Introduction:-

Synonyms:-Saffron Indian; haldi (Hindi): Curcuma; Rhizoma cur-cumae.

Biological Source: Curcumin is the main active ingredient of turmeric, a spice obtained by grinding the dried rhizomes of the plant Curcuma longa Linn. (syn. C.domesticaValeton)., belonging to family Zingiberaceae[7][8] [9]

Description:- Turmeric dry rhizome is composed mainly of the starch, having also carbohydrates, proteins, lipids, fiber, curcuminoid pigments, sesquiterpenes and caffeic acid [10,11]" The curcuminoid content typically varies between 2% and 9%. Curcumin is the most abundant curcuminoid in turmeric, but traces of its precursors, desmethoxycurcumin and bisdemethoxycurcumin are also present.[12]

Chemical Constituents: -

Turmeric contains about 5% flexible oil, amber, large amount of zingiberaceous starch and yellow substances known as curcuminoids. The main component of curcuminoids is known as curcumin (50-60 percent). Chemically, the Curcuma varieties contain hot oils, starch and curcumin. Curcumin and other related curcuminoids such as Demethoxycurcumin and Bis Demethoxycurcumin are reported to be responsible for the yellow colour in some species. The oil content varies from 1-6.5 percent and is made of mono and sesquiterpene such as A and B pinene, phellandrene, camphor, camphene, DL-ar-turmerone stain and a, ß curcumenes. Types such as C. angustifolia and C. caulina have high starch and are used instead of the root of the arrow.

Chemical test:-

1) Turmeric powder on treatment with concentrated sulphuric acid forms red Colour.
2) On addition of alkali solution to turmeric powder red to violet colour is produced.
3) With acetic anhydride and concentrated sulphuric acid turmeric gives violet colour. Under UV light this colour is seen as an intense red fluorescence.
4) A paper containing turmeric extract produces a green colour with borax solution.
5) On addition to boric acid a reddish-brown colour is formed which, on addition of alkalis changes to greenish-blue.

Chemistry of curcumin-

Chemical formula of the curcumin is the $C_{21}H_{20}O_6$. It is also referred to as diferuloylmethane, having a very long IUPAC denomination: (1E,6E)-1, 7-bis (4- hydroxy-3methoxyphenyl)-1, 6-heptadiene-3,5dione.

Its chemical structure comprises two aromatic ring systems with o-methoxy phenol groups connected by a seven-carbon linker consisting of a, B-unsaturated ß-diketone moiety that exhibits keto-enol tautomerism in solution. [13]

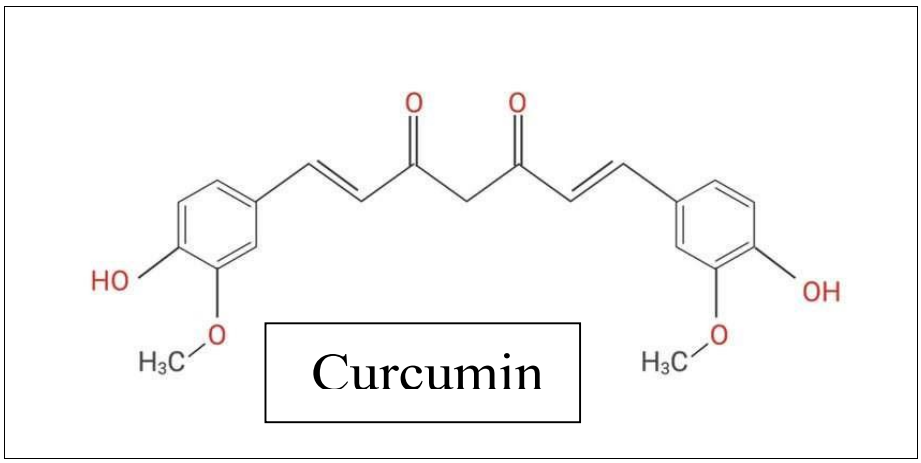
Due to extended conjugation, the x electron cloud is distributed all along the molecule making curcumin very hydrophobic, with a log p value of 3.38 and an extremely low solubility in water (1.34 ± 0.02 mg/L) [14]. Curcumin is reasonably stable in water at pH < 7.0 due to structural stabilization by the conjugated diene; in PBS and at pH > 8 it may degrade rapidly (10 min). In fact, cur cumin possesses three ionisable protons with pKa values of approximately 8.5 (enolic proton) and 10-10.5 (two phenolic protons). [15]

Curcumin absorbs light from the near ultraviolet (around 340 nm) to the indigo-blue spectral region (450-460 nm), with absorption peaking at 410-430 nm (violet light). It presents a fluorescence band between 460 and

560 nm. Furthermore, curcumin is sensitive to ultraviolet radiation and its degradation is accelerated by exposure to sunlight. [16,17]

When irradiated with light above 400 nm, curcumin undergoes a self-sensitized photo- decomposition where singlet oxygen is involved, but when reactive oxygen species are not available, other decomposition mechanisms are triggered. Photo degradation products include vanillin, vanillic acid, 4-vinyl-guaiacol, ferulic aldehyde, and ferulic acid. [18]

STRUCTURE OF CURCUMIN



Structure of Curcumin [19]

Extraction of Curcumin and detection-

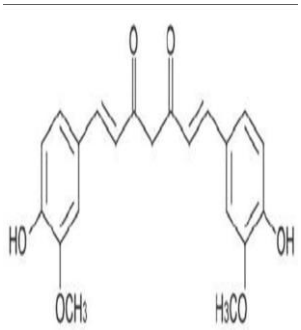
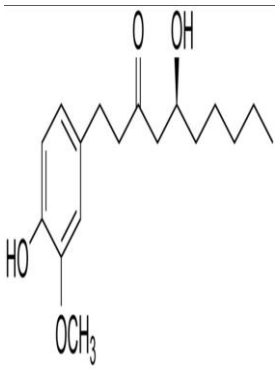
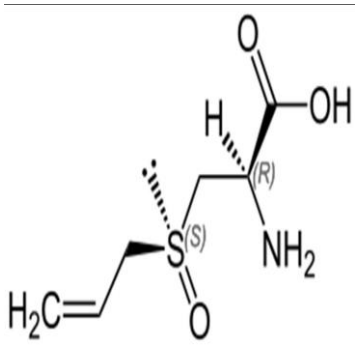
The largest worldwide producer of turmeric is India, where it has been used as a homeremedy for several ailments for ages. Depending on its origin and the soil conditions where it is grown, turmeric contains 2%-9%curcuminoids[20] The word "curcuminoid" indicates a group of compounds such as curcumin, demethoxycurcumin and bis-demethoxycurcumin and cyclic curcumin. Out of these, curcumin is the major component, and cyclic curcumin is the minor component.

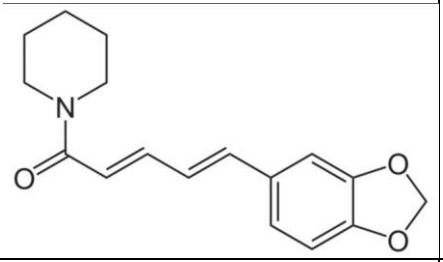
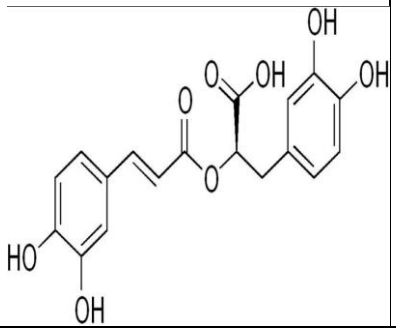
Solvent extraction followed by column chromatography has been the most commonly employed method reported. Soxhlet extraction, ultrasonic extraction, microwave, zonerefining and dipping methods have been tried, and among these the Soxhlet, ultrasonic and microwave extractions are the most commonly employed methods.[21]Recently pulse ultrasonic and microwave-assisted extraction methods have also been reported to be better than the continuous methods. Being free from organic solvents, pilot plants based on supercritical carbon dioxide have been established in several countries for the extraction of curcumin from turmeric. There are also a few reports on enzyme-assisted extraction, where pre-treatment of turmeric with enzymes like a-amylase and glucoamylase yielded significant increases in curcumin yield. [22]

Curcumin can be separated from curcumin mix (a mixture of curcumin, demethoxycurcumin and bisdemethoxycurcumin) by column chromatography by adsorbing the mixture on silica gel using mixtures of solvents like dichloromethane/acetic acid or methanol/chloroform to yield three different fractions. The curcumin fraction is further purified on silica gel using chloroform/dichloromethane and ethanol/methanol mixtures as eluents Methods for the detection and estimation of curcumin have mostly employed the high performance liquid chromatography (HPLC) technique. In general reverse phase C18 columns are used as stationary phase and different gradients of solvents containing acetonitrile/water or chloroform/methanol have been employed as the mobile phase. [23]

For detection of curcumin, in the wavelength range from 350 to 450 nm range or in the UV region using a common detection wavelength in the range of 250 to 270 nm. Liquid chromatography-coupled mass spectrometry has been another versatile tool for detecting curcumin. Micro emulsion electro kinetic chromatography using oil droplets and surfactants has been found to be good for both extraction and estimation of curcumin in food and medicinal samples. Capillary electrophoresis with amperometric detection can be routinely employed to estimate curcumin/turmeric in food materials. Ultra-performance liquid chromatography (UPLC) coupled with online tandem mass spectrometry has been used to detect curcumin metabolites in plasma and urine, with detection limits of 2.5 mg/mL [24]

SPICE PHYTOCONSTITUENT AS A ANTIINFLAMMATORY AGENTS TABLE

S R. NO.	SPICE CHEMICALS	SOURCE	STRUCTURE	REFERENCE
01	TURMERIC	Curcuma longa		Turmeric: The genus Curcuma. Edited by P. N. Ravindran, K. NirmalBabu, K. Sivaraman. Boca Raton : CRC Press, 2007. "Curcuma longa L." Plants of the World Online, Kew Science, Kew Gardens, Royal Botanic Gardens, Kew, England. 2018. Retrieved 26 March 2018.
02	GINGER	Zingiber officinale		"Zingiberofficinale". Germplasm ResourcesInformation Network (GRIN). AgriculturalResearch Service (ARS), United StatesDepartment of Agriculture (USDA). Retrieved 10 December 2017.
03	GARLIC	Allium sativum		"Allium sativum L". Kewscience; Plants of the World Online; RoyalBotanic Gardens, Kew, England. Retrieved May 26, 2017.

04	BLACKPEPPER	Piper nigrum L.		"Piper nigrum". Germplasm ResourcesInformation Network (GRIN). AgriculturalResearch Service (ARS), United StatesDepartment of Agriculture (USDA). Retrieved 2 March 2008.
05	ROSEMARY	Rosmarinus officinalis		"Rosmarinusofficinalis(rosemary)". Centre for Agriculture and Bioscience International. 3 January 2018. Retrieved 13 July 2018

ADVANTAGE AND DISADVANTAGE OF TURMERIC
ADVANTAGE

1) SUPPORT IMMUNE HEALTH
2) HELP IN WOUND HELAING
3) IT PROMOTE WEIGHT LOSS
4) IT IMPROVE DIGESTION
5) IT HELP IN RELIEVE PAIN

DISADVANTAGE

1) It may help reduce the risk of cancer
2) It thins your blood
3) Blood-thinning effects alone, pregnant women should avoid taking turmeric supplements. Adding small amounts of turmeric as a spice to food shouldn't be a problem. 4) It can upset your stomach. [25]

PHARMACOKINETICS & PHARMACODYNAMICS

Previous studies have been discussing the difficulty in achieving optimum therapeutic concentrations of the molecule due to poor bioavailability and low solubility of curcumin. Studies intimate that the curcumin is first bio transformed to dihydrocurcuminand tetrahydrocurcumin, and subsequently converted to monoglucuronide conjugates. [26]

While the anti-oxidant and anti-inflammatory effects of curcumin, a natural product present in the roots of Curcuma longa have been studied widely, the acute pharmacokinetics (PK) and pharmacodynamics (PD) of curcumin in suppressing pro-inflammatory markers and epigenetic modulators remain unclear [27]

Animal studies show the curcumin is rapidly metabolized and conjugated in the liver, and then excreted in faces with limited systemic bioavailability. A 40 mg/kg IVdose of curcumin given to rats resulted in complete plasma clearance at one hour post-dose. An oral dose of 500 mg/kg given to rats resulted in a peak plasma concentration of only 1.8 ng/mL. [28]

A method that has been employed to increase the bioavailability of curcumin that means it is use agents that block the metabolic pathway of curcumin.
Pharmacokinetic and bioavailability is the studies of curcumin have been indicated its low intestinal absorption and rapid clearance from the body. Absorption, Metabolism, Bio distribution and excretion of curcumin in rodents

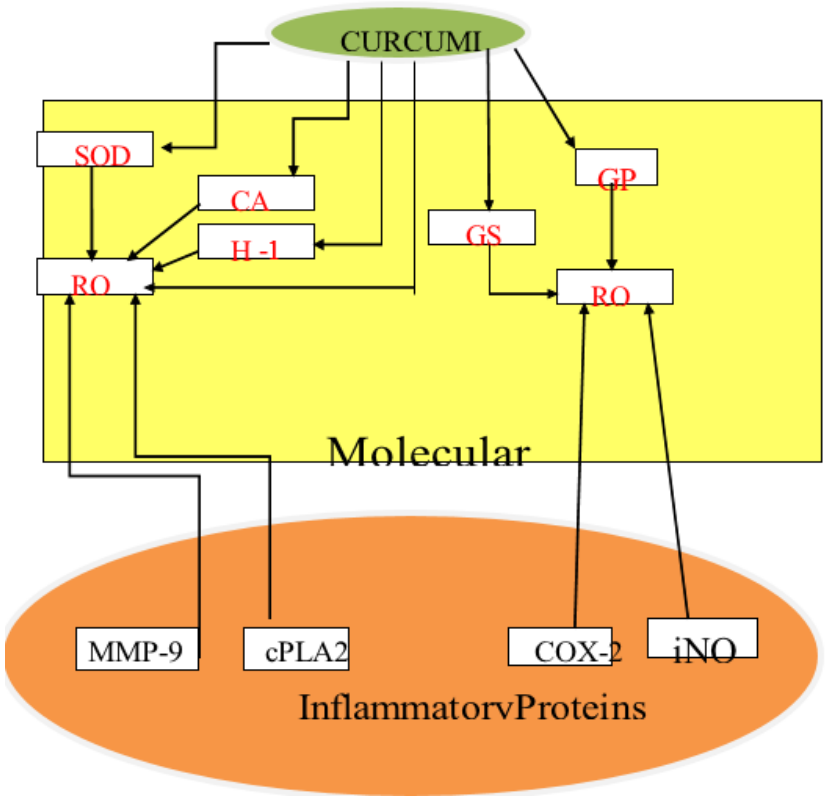
have been reported in several studies [30].The overall findings imply that curcumin has a low absorption and rapid clearance following oral use. In a primary research, a dose of 1 g/kg curcumin was administered to rats and resulted in about 75% excretion of curcumin[.Various phase I clinical trials report data on the systemic bioavailability and pharmacokinetics, metabolites, of curcumin in humans.
Another study of 24 patients aimed to specify levels of curcumin and its metabolites in colorectal mucosa of patients rather than measuring serum concentration. [29]

Curcumin C3-complex (2.35 g) was administered daily for 14 days prior to endoscopic biopsy or colonic resection. Curcumin and its metabolites were detectable in 9/24 plasma samples, 24/24 urine samples and in the colonic mucosa of all 23 biopsied participants with mean tissue levels at 48.4 μg/g. The only adverse event reported was mild abdominal discomfort in 06 patients, and 67% expressed acceptability of the therapy long-term should it be of proven benefit. [27]Nitrite levels, which are regulated by inducible nitric oxide synthase (iNOS), play a critical role in inflammation
In summary, the Pharmacokinetics and Pharmacodynamics modeling approach could potentially provide a robust quantitative framework for evaluating the acute antiinflammatory and epigenetic effects of curcumin in future clinical trials.

MECHANISM OF ACTION OF CURCUMIN AS THE ANTIINFLAMMATORY AGENTS

Abbreviations

GPx- Gluthathione Peroxidase
SOD- Superoxid Dismutase
CAT- Catalase
HO-1- Heme Oxygenase1
GST- Gluthathione S Transferase
MMP-9- Matrix Metallo Proteinase9
cPLA2 Cytosolic Phosholipase A2
COX-2 Cyclooxygenase 2
iNOS Inducible Nitric Oxide Synthase
ROS Reactive Oxygen Species



ADVERSE EFFECT

- Digestive issues. People may experience mild digestive issues such as acid reflux, bloating and diarrhoea at daily doses exceeding 1,000 mg
- Nausea & Headache Doses of 450 mg or higher may cause headache and nausea in a small number of people.
- Skin rash. After taking a dose of 8,000 mg of curcumin People have reported a skin rash. But this seems to be very rare. [31]

- Such as allergic reactions
- Vomiting
- Stomach pain
- Constipation
- Diarrhoea
-

Potential Risks & Side Effects

As a cooking spice, turmeric is extremely safe. However, at the higher doses used in some experimental treatments (1,500 to 2,000 milligrams a day), it has the potential to cause issues in some people, including:

- Clotting problems. Turmeric may slow blood clotting, which can create problems major injury or post-surgery. This effect also means that people taking prescription blood thinners and they should avoid high doses of turmeric.

- Iron deficiency. In liable patients in one study, high doses interfered with iron metabolism.

- Kidney stones. Turmeric naturally contains oxalates, organic acids that increase the risk of kidney stones formation in people who are prone to them.

- Nausea and other gastrointestinal distress.

RECENT RESEARCH OF THE TURMERIC

Turmeric, a shrub related to ginger, is grown throughout India, other parts of Asia, and Africa. Known for its warm, bitter taste and golden colour, turmeric is commonly used in fabric dyes and foods such as curry powders, mustards, and cheeses. In traditional Chinese medicine turmeric has been used to aid digestion and liver function, relieve arthritis pain, and regulate menstruation. Turmeric has also been applied directly to the skin for eczema and wound healing. Today, turmeric is used for conditions such as heartburn, stomach ulcers, and gallstones. It is also used to reduce inflammation, as well as to prevent and treat cancer.

SIDE EFFECT OF CURCUMIN-

It is important to remember that turmeric used in cooking is very safe. But we don't know how safe cur cumin is when used for medical reasons. So far, research studies seem to show that it causes few or no side effects. But we don't know much about the side effects of taking it in large amounts to treat or prevent cancer.

FurtadoL contains the strong anti-inflammatory drug nimesulide. Nimesulide can cause severe damage to the liver. The signs include:

- Yellowing skin (jaundice)
- Dark urine
- Feeling or being sick
- Unusual tiredness
- Stomach or abdominal pain
- Loss of appetite

FUTURE STUDIES AND PERSPECTIVES

In this review, we highlighted the importance of curcumin as an anti-inflammatory compound

In the future, we will explore the mechanism by which curcumin-induced up regulation of PPAR-γ leads to the suppression of TNF-α release to provide protection in sepsis.

. In vitro studies with macrophages are recommended to dissect the precise mechanism of curcumin-induced anti-inflammatory effects

Prior studies on the anti-inflammatory nature of curcumin were done on curcumin itself. Further studies with curcumin metabolites, curcumin sulphate, and curcumin glucuronide will warrant answering such questions.

The effect of curcumin on other models of tissue injury should also be explored. Thus, more in vitro and preclinical researches are needed to render curcuminor its metabolites as therapy for sepsis and/or other models of tissue injury peroxisome proliferator-activated receptor-γ (PPAR-γ)

II. CONCLUSION

In the light of above facts, it can be concluded that the Turmeric (Haridra) has a lot of potentials when it comes to its medicinal usage.

Turmeric has broad spectrum actions with certain effects and is beneficial for long term and daily usage. Turmeric is an auspicious beauty agent, daily applied on the forehead by Hindu females. Turmeric is the household spice for diverse cuisines in all parts of India since many centuries. Generally the rhizome powder of Turmeric is used as a spice all over India but only a few people are aware of its therapeutic properties. Turmeric is regarded as one of the best drug in many diseases like Diabetes, Skin diseases etc., which is in use since ages owing to its multiple pharmacological activities. Turmeric is enriched with many useful phytoconstituents which are responsible for its efficacy. Curcumin is one such phytoconstituent, a nutraceutical substance with numerous pharmacological activities proven experimentally and clinically. It has been established beneficial in treating Antiinflammatory, Anti-allergic, Anti-oxidant, Anti-hyperglycaemic and Anti- cancer properties. Till date many researches have been carried out on the medicinal effects of Turmeric, this review will give a new impetus to utilise turmeric in various disorders.

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