

WORLD JOURNAL OF PHARMACEUTICAL RESEARCH

SJIF Impact Factor 8.084

Volume 12, Issue 1, 710-727.

Review Article

ISSN 2277-7105

TURMERIC- A REVOLUTION ON PHYTOMEDICINE

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Article Received on 10 Nov. 2022,

Revised on 30 Nov. 2022, Accepted on 20 Dec. 2022

DOI: 10.20959/wjpr20231-26703

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ABSTRACT

Flavonoids, tannins, glycosides, alkaloids, and terpenoids are examples of phytoconstituents with medical benefits. Herbal medications have been produced in recent years and are used to treat practically all ailments with minimal or no adverse effects. Asiatic culture and cuisine are inextricably linked to turmeric (Curcuma longa L.). It is said to provide a wide range of health advantages. The most physiologically active curcuminoid found in turmeric, curcumin, is being studied in pre-clinical and clinical studies for its potential to treat and prevent illness. The usual method for obtaining turmeric's health

benefits is through long-term, low-dose food ingestion. For turmeric to be used rationally in the treatment of human illnesses, a detailed understanding of the effective dosage, safety, and mechanism of action is necessary. If turmeric is to be used for addressing human needs and enhancing human wellbeing, more clinical investigations are required. Turmeric has a number of beneficial effects on the body, including digestive, antibacterial, antiviral, anti-inflammatory, anti-tumor, antioxidant, and antiseptic properties. The development of a revolutionary herbal medication delivery method termed a phytosome, which increases the bioavailability and absorption of bioactive components, has had a significant impact on the health care system. Turmeric phytochemical analysis. The innovative medication delivery mechanism is carried by phytosomes.

KEYWORDS: Turmeric, Anti-inflammatory, Phytochemical, Phytosomes.

INTRODUCTION

Throughout human history, natural plant products have been employed for a variety of reasons. Many of the plants that give rise to these natural chemicals are billions of years old, having co-evolved with animal life.^[1,2] Tens of thousands of these products are created as

www.wjpr.net Vol 12, Issue 1, 2023. ISO 9001:2015 Certified Journal 710

secondary metabolites by higher plants as a natural defensive mechanism against illness and infection. Many of these natural compounds contain pharmacological or biological properties that can be used in the discovery and creation of pharmaceutical drugs. [3] Plant-based medicines have been essential to the health care of many societies, both ancient and contemporary. Ayurveda, an Indian holistic medical approach, primarily employs plant-based medications or formulations to treat a variety of illnesses, including cancer. [4] Although many synthetic drugs are created using combinatorial chemistry, plant-based drugs are more suitable, at least in terms of biochemistry, for human use. Of the at least 877 small-molecule drugs introduced worldwide between 1981 and 2002, the origins of the majority (61%) can be traced to natural products. However, neither has modern medicine promoted nor placed a high value on using natural items for medical purposes. The usage of the turmeric plant for medical purposes dates back over 4000 years. Turmeric is utilised in Southeast Asia both as a primary spice and as a part of religious rituals. In vitro studies with turmeric are covered first, followed by animal studies, then human studies; the safety and efficacy of turmeric are also addressed. Turmeric is also known as "Indian saffron" because of its brilliant yellow colour. Modern medicine has started to recognise its importance, as shown by the over 3000 publications dealing with it that have appeared in the last 25 years. [6] This review first covers in vitro studies with turmeric, then moves on to animal studies, then human studies.

Origin, Nomenclature, History, Cultivation, and Processing of turmeric

The usage of turmeric stretches back over 4000 years to the Vedic period in India, when it was employed as a culinary spice and had some religious importance. It probably reached China by 700 ad, East Africa by 800 ad, West Africa by 1200 ad, and Jamaica in the eighteenth century. Marco Polo wrote about this spice in 1280, astonished at a vegetable with characteristics so close to saffron. Turmeric has a long history of medical usage in South Asia, according to Sanskrit medical texts, Ayurvedic, and Unani traditions. Susruta's Ayurvedic Compendium, which dates back to 250 BC, suggests using a turmeric-containing salve to treat food poisoning. [7,8]

Today, turmeric is grown extensively throughout the tropics and is known by several names in various cultures and nations. The name turmeric comes from the Latin terra merita (meritorious earth), referring to the colour of ground turmeric, which resembles a mineral pigment. In North India, turmeric is frequently referred to as "haldi," a word derived from the Sanskrit word haridra, and in the south, it is known as "manjal." In various languages, it is

referred to as "yellow root" or simply "terre merite." [10,11] Its name is derived from the Latin word curcuma in numerous civilizations. There are at least 53 different names for turmeric in Sanskrit, including anestha (not offered for sacrifice or homa), bhadra (auspicious or lucky), bahula (plenty), dhirgharaja (long in appearance), gandhaplashika (which produces good smell), gauri (to make fair), gharshani (to rub), haldi (that draws attention to its bright colour), haridra (dear to hari, Lord. [12,13]

Curcuma longa, a rhizomatous herbaceous perennial plant native to tropical South Asia and a member of the ginger family Zingiberaceae, produces turmeric. Around the world, 133 different species of Curcuma have been discovered. The majority of these species go by popular local names and are utilised in a variety of pharmaceutical preparations. The turmeric plant requires temperatures between 20°C and 30°C as well as a sizable quantity of yearly rainfall to flourish. Some particular turmeric species are shown here. Individual plants have long, oblong leaves and can reach a height of 1 m. Plants are harvested yearly for their rhizomes, and part of those rhizomes are used to reseed the next season. The turmeric's source plant, the rhizome, is tuberous and has a rough, segmented skin. [14] In the ground, the rhizomes develop beneath the leaf. They have a dull orange inside and a yellowish brown outside. Smaller tubers branch off from the main rhizome, which is pointed or tapered at the distal end and measures 2.5-7.0 cm (1-3 inches) in length and 2.5 cm (1 inch) in diameter. The rhizome of the turmeric plant, Curcuma longa, which is native to tropical South Asia and is a perennial herbaceous plant with rhizomes, may be dried and processed into a yellow powder with a bitter, somewhat acrid, yet sweet flavour. Around the world, 133 different species of Curcuma have been discovered. The majority of these species go by popular local names and are utilised in a variety of pharmaceutical preparations.^[15] The turmeric plant requires temperatures between 20°C and 30°C as well as a sizable quantity of yearly rainfall to flourish. Some particular turmeric species are shown here. Individual plants have long, oblong leaves and can reach a height of 1 m. Plants are harvested yearly for their rhizomes, and part of those rhizomes are used to reseed the next season. The rhizome, which is tuberous and has a rough, segmented skin, is where turmeric is obtained. In the ground, the rhizomes develop beneath the leaf. They have a dull orange inside and a yellowish brown outside. The main rhizome is 2.5-7.0 cm (1-3 inches) in length and 2.5 cm (1 inch) in diameter, with smaller tubers branching out. It is pointed or tapered at the distal end. The dried turmeric rhizome may be processed into a yellow powder that has a bitter, almost acrid, yet sweet flavour.[16]

India produces almost all of the turmeric crop in the world and uses 80% of it. Indian turmeric is regarded as the greatest in the world due to its natural properties and high level of the significant bioactive component curcumin. The greatest production and most significant trade hub for turmeric in the world is Erode, a city in the South Indian state of Tamil Nadu. India produces almost all of the turmeric crop in the world and uses 80% of it. Indian turmeric is regarded as the greatest in the world due to its natural properties and high level of the significant bioactive component curcumin. The greatest production and most significant trade hub for turmeric in the world is Erode, a city in the South Indian state of Tamil Nadu. Sangli, a city in Maharashtra, is second only to Erode in terms of size and significance as a hub for the production and commerce of turmeric. [It is also known as "Yellow City," "Turmeric City," or "Textile City.".

Composition of turmeric

Turmeric has more than 100 components that have been identified. Turmeric contains other colouring agents known as curcuminoids, including curcumin demethoxycurcumin, 5'-methoxycurcumin, and dihydrocurcumin, which have been discovered to be natural antioxidants. The major component of the root is a volatile oil that contains turmerone. Curcumin (5–6.6%), extraneous matter (0.5% by weight), mould (3%), and volatile oils (3.5%) are all present in turmeric in conventional form, along with moisture (>9%). D-phellandrene, d-sabinene, cinol, borneol, zingiberene, and sesquiterpenes are examples of volatile oils. There are several sesquiterpenes, many of which are unique to a particular species, including germacrone, termerone, ar-(+)-, -, and -termerones, zingiberene, sesquiphellanderene, bisacurone, curcumenone, dehydrocurdione, procurcumadiol, bisacumol, curcumenol, isoprocurcumenol Turmeric's scent is attributed to turmerone, arturmerone, and zingiberene. The rhizomes are also said to include four novel polysaccharides, known as ukonans, as well as cholesterol, stigmasterole, -sitosterole, and 2-hydroxymethyl anthraquinone.

Consumption and Importance of turmeric

Uses for turmeric include food, cosmetics, and medicinal. It is a common spice in Middle Eastern and South Asian cuisine. Curry's unique yellow colour and flavour come from it. In cheese, butter, and other foods, it serves as a colouring agent. Turmeric has gotten into Ethiopian food as a result of Indian influence. Turmeric has long been used in South Africa to tint boiling white rice a golden hue. Additionally, turmeric is utilised in processed foods

including gelatins, canned beverages, dairy products, baked goods, ice cream, yellow cakes, yoghurt, orange juice, biscuits, popcorn, candies, and cake icings. It is a key component in the majority of branded curry powders. Asian cuisine use turmeric in a variety of ways.^[24]

Some estimates place the annual cost of alternative medicines at up to \$10 billion USD. Spending on botanical supplements for conditions including chronic obstructive pulmonary disease (COPD), asthma, and rheumatoid arthritis exceeds \$650 million, according to the USDA. In traditional medicine, including Ayurveda (the science of long life), Chinese medicine, Kampo (Japanese medicine), and Egyptian medicine, botanical supplements have been utilised for millennia. Many of the conventionally prescribed medications include anti-inflammatory properties. One such herb is turmeric. [25]

Turmeric as a traditional medicine

Over the years, turmeric has been employed in various sections of the world's traditional medicine in medicinal concoctions. Turmeric is used as an antiseptic for wounds, burns, and bruises as well as an antibacterial agent in many South Asian nations. It is also believed to have several medical benefits in Ayurvedic techniques, including boosting the body's general vitality and alleviating colic, worms, and arthritis. It is employed as an anti-inflammatory medication as a treatment for digestive discomfort brought on by irritable bowel syndrome and other digestive illnesses in Pakistan. [27,28]



Figure 1: Health benefits of turmeric.

Clinical studies using turmeric

A number of human ailments have been tested against by turmeric. The antimutagenic properties of turmeric were investigated in one research, which involved 16 chronic smokers. [29] Turmeric was administered at dosages of 1.5 g/day for 30 days, and it was discovered that this considerably decreased the urine excretion of mutagens in these smokers. On the other hand, there was no difference in the urine excretion of mutagens among six non-smokers. These findings imply that turmeric consumption is a potent antimutagen and may aid in chemoprevention. Another research looked at how people with irritable bowel syndrome responded to turmeric. [30]

Safety, Efficacy and Contraindications

Since ancient times, turmeric has been used both as a spice and a common home treatment with no known adverse effects. It is evident that turmeric is not harmful even at extremely high levels because no research in either people or animals have found any toxic consequences related to its usage (Lao et al., 2006). With regard to turmeric, the American Food and Drug Administration (FDA) has carried out its own clinical studies and released a 300-page monograph. The active ingredient in turmeric, curcumin, has been deemed GRAS by the FDA (generally regarded as safe). [31]

From traditional medicine to modern medicine

Although it has been used often to treat a variety of disorders, modern medicine is just a few decades old. In contrast, traditional medicine has helped people for thousands of years and is both safe and effective. Traditional medicine's mechanism or scientific foundation, however, is less well known.^[32]

Phytosomes

The vesicular drug delivery system known as phytosomes (or herbosomes) increases the absorption and bioavailability of low-soluble drugs.^[33,34] Phytosomes are complexes of phospholipids and naturally occurring active phytochemicals, bound in their structures, and produced by the reaction between phosphatidylcholine (or any hydrophilic polar head groups) and plant extracts in an aprotic solvent. The hydrophilic phytoconstituent-choline complexes are entirely covered by the lipid-soluble phosphatidyl part. High drug encapsulation, better stability (chemical bonds are formed between the polar head of the amphiphile molecule and the phytoconstituent), and better bioavailability are just a few of the impressive advantages of

phytosomes.^[37] Additionally, a higher absorption rate results in a lower dosage of active constituents for exerting a biological effect, also for polar phytoconstituents.^[38]

Bombardelli et al stated that first evidence of a chemical link between phospholipids and molecules of flavonoid vegetal derivatives was provided by Pu et al in 2016 when they looked at a molecular docking model for the interaction of 20(S)-protopanaxadiol (PPD) phospholipid complexes. According to the findings, the phospholipid molecule's two hydrophobic arms encircle the PPD framework's hydrophobic section, and one of the hydrophilic-OH groups creates a hydrogen connection with the P=O section's phospholipid backbone. [40]

Properties of phytosome

In most cases, a phytosome is a polyphenolic molecule connected to at least one phospholipid molecule. A phytosome can range in size from 50 nm to several hundred nm. When exposed to water, phytosoms take on a micellar form resembling a liposome. Phytosome complex often freely soluble in aprotic solvents, moderately soluble in fats, insoluble in water, and relatively unstable in alcohol. Phytosomes express their behaviour in physical or biological system due to their physical size, membrane permeability, percentage entrapment, chemical composition, quantity, and quality of the materials used. With the aid of a hydrogen bond between the phenolic hydroxyl end of polyphenols and their phosphate ion phosphatidylcholine (phospholipid) moiety, the phytoconstituent in phytosomes is connected to the polar head of phospholipid. As a result, phytoconstituents are now an essential component of the phytosome membrane. The lipophilic envelop of phytosomes protects the polar heads of the polyphenolic and phospholipid molecules and enables the complex to dissolve in low polarity solvents, improving the phytoconstituent's absorption and bioavailability. All phytoconstituent's absorption and bioavailability.

Difference between Phytosomes and Liposomes

In a liposome, the hydrophillic drug molecule is trapped in the cavity or spaces between the membrane, whereas in a phytosome, the hydrophillic herbal drug molecule is linked with the polar head of the phospholipid. A comparison of phytosomes and liposomes in^[43] shows that while conventional liposomes lack chemical bonds, phytosomes have hydrogen bonds that bind the phenolic hydroxyl end of the phytoconstituent molecule to the polar head Phosphatidylcholine molecules may number in the hundreds of thousands and surround the water-soluble substance in the liposome. In contrast, depending on the components

complexed, phosphatidylcholine and a plant ingredient really create molecular complexes. Better bioavailability and absorption of phytosomes are the effects of this.^[44]

Preparation method of phytosomes

Phytosomes are created by mixing a synthetic or natural phospholipid with a standardised plant extract in a ratio ranging from 0.5 to 2.0 (1:1 is preferred) in an aprotic solvent, such as dioxane, methylene chloride, or acetone. From there, a novel complex can be isolated by precipitation with a non-solvent, typically an aliphatic hydrocarbon, or by lyophilization or by spray drying. While aprotic solvents including dioxane, acetone, and mrthylene chloride are utilised to prepare phytosomes, other procedures are also employed to create dipalmitoyl phosphatidylcholine and distearyl phosphatidylcholine:

- Antisolvent Precipitation Technique
- Co- Solvent Lyophilisation Method
- ➤ Thin Layer Hydration Technique
- ➤ Solvent Evaporation Technique

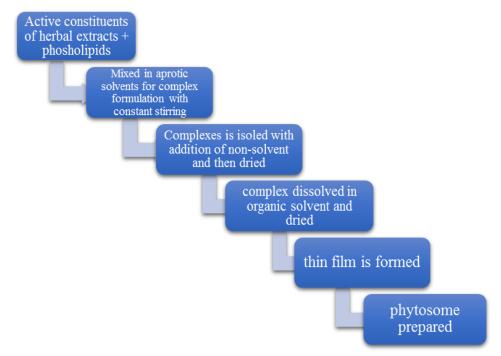


Figure 2: Preparation of phytosomes.

Antisolvent precipitation technique

A particular amount of medication and phospholipid are refluxed with the appropriate solvent in the Antisolvent Precipitation Technique. After the mixture has been concentrated, another solvent is added, and the mixture is continuously stirred to allow for precipitation. The resulting precipitates are then collected, filtered, and overnight kept in vacuum desiccators.^[47]

Co- Solvent Lyophilisation method

The medication and the phospholipid are each individually dissolved in a suitable solvent in the co-solvent lyophilisation technique. The two are then gently stirred together until a clear mixture forms. The resulting homogenous solution is then vacuum-freeze dried and kept in an airtight container.^[48]

Thin layer hydration technique

Cholesterol is dissolved in dichloromethane whereas phytoconstituents and phosphatidylcholine are dissolved in methanol in the thin layer hydration procedure. In a rotary evaporator, the mixture is evaporated until a thin, dry layer is created. To completely remove organic solvents, nitrogen gas is blasted over a thin film. Then, distilled water is used to hydrate the film.^[49]

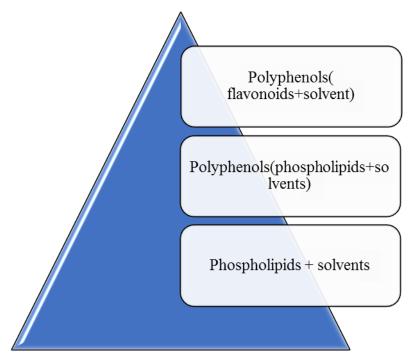


Figure 3: Thin-film hydration as the most common method for phytosome preparation. Solvent evaporation technique.

The medication and the phospholipids are typically both put in the same flask and refluxed with a suitable solvent at a certain temperature for a set amount of time when using the solvent evaporation procedure. In a round bottom flask, the precise quantity of

phytoconstituent and soy lecithin are added, and they are refluxed with acetone at a temperature of $50-60^{\circ}$ C for two hours.^[50]

Characterization and Evaluation of phytosomes

On phytosomes, many in-vitro and in-vivo evaluations are used. Models for in-vitro and in-vivo evaluations are chosen based on the anticipated therapeutic activity of biologically active phytoconstituents present in the Phytosome characterization is done by physical attributes like shape, size, distribution, drug entrapment capacity, drug release, membrane permeability; and chemical composition which govern the action of phytosome in both physical and biological system.

Visualization

Microscopic view

The phytosome complex was characterised using optical microscopy. A drop of the complex was put on a glass slide and covered with a coverslip while the complex was submerged in water. Under various magnifications, a phytosome was seen in a microscopic perspective.^[51]

Transmission Electron Microscopy (TEM)

A beam of electrons is transmitted through a material to create a picture in the microscopy method known as transmission electron microscopy (TEM). Most frequently, the specimen is a suspension on a grid or an ultrathin slice that is less than 100 nm thick. As the beam passes through the specimen, a picture is created as a result of the electrons' interactions with it. An imaging device, such as a fluorescent screen, a sheet of photographic film, or a sensor like a scintillator linked to a charge-coupled device, is then used to magnify and focus the picture. A morphological analysis of the produced phytosomes was conducted. The sample was made by centrifuging the phytosomal dispersion, which was then applied to a copper grip coated with carbon. A thin film was then left, dried, and the mean particle size of the vesicle was then examined. [52]

Scanning Electron Microscopy (SEM)

A concentrated electron beam is used to scan a sample's surface in a scanning electron microscope (SEM), which creates pictures of the sample. The sample's surface topography and chemical composition are revealed by the signals that are created as a result of the electrons' interactions with the sample's atoms. An picture is created by combining the position of the electron beam with the strength of the signal being detected as it is being

scanned in a raster scan pattern. A secondary electron detector is used in the most popular SEM mode to find secondary electrons released by excited atoms (Everhart–Thornley detector). The topography of the specimen is one factor that affects the quantity of secondary electrons that may be detected and, consequently, the signal strength. The resolution of some SEMs can exceed 1 nanometer. In order to ascertain the surface morphology, size, and form of the phytosomes, a scanning electron microscopy investigation was conducted.^[53]

Measurement of particle size

- A particle size analyser was used to calculate the phytosomes' particle size. 100 l of the sample were diluted with the necessary amount of distilled water to determine the particle size, and the diameter of the vesicle was measured.
- Additionally, the poly dispersible index may be evaluated using the photon correlation spectroscopy (PCS) method, which is also utilised to validate the vesicular structure and investigate the size of phytosomes.^[54]

Vesicle Size and Zeta potential

The electrical potential at the sliding plane is known as zeta potential. The interface that divides fluid that is mobile from fluid that is still affixed to the surface is this plane.

Electrokinetic potential in colloidal dispersions is known scientifically as zeta potential. It is often represented in the literature on colloidal chemistry by the Greek symbol zeta (), therefore "potential." The standard units are millivolts (mV) or volts (V) (mV). The electric potential in the interfacial double layer (DL) at the site of the sliding plane in relation to a point in the bulk fluid distant from the interface is known as the zeta potential from a theoretical perspective. Zeta potential, in other terms, is the potential difference between the stationary fluid layer linked to the dispersion medium and the Vesicle size and zeta potential were determined using dynamic light scattering (DLS), a computerised inspection system, and photon correlation spectroscopy (PCS).^[55]

Surface tension measurement

In order to break a film with a length of 1 cm, surface tension is commonly measured in dynes/cm. According to the definition of surface tension, the gas, solid, or liquid in contact with the provided liquid, as well as the forces of attraction between the particles inside it, are the key determinants of surface tension. The drug's surface tension in an aqueous solution was measured using the ring technique in a dunuoy ring tensiometer.^[56]

Spectroscopic evaluation

NMR Studies (Nuclear magnetic resonance)

It is a useful tool for understanding molecular structure. Based on the information, it is possible to deduce that phytosome production occurs. It also aids in understanding the electron distribution in molecules and the quantum mechanical basis of bonds. such as H1-NMR and 13C-NMR.^[57]

FTIR Studies (Fourier Transformed Infra-red Spectroscopy)

The structure and chemical stability of phytosome-loaded phospholipid, polymer, and medication samples may be assessed using FTIR spectrum data. At a pressure of 600 kg/cm2, the sample can be crushed with potassium bromide (KBr) to produce pellets. Spectral scanning is possible between the wavelengths of 4000-400cm⁻¹.^[58]

Entrapment efficiency

Weighing the entire batch is the first step in determining the entrapment efficiency; this weight is referred to as the recovered mps. One gramme was lost in the manufacturing process. The separation technique should be quick and easy, and it's best to minimise diluting of the samples too much and medication loss from the liposome's inside. Both the direct and indirect methods may be used to determine the entrapment effectiveness of nanocarriers. The last one gramme wasted in manufacturing is one of the elements affecting defect entrapment efficiency. Weighing the entire batch is the first step in determining the entrapment efficiency; this weight is referred to as the recovered mps. The phytosomal preparation was centrifuged for the designated amount of time using a cooling centrifuge at 4 °C and high rpm. After carefully separating the clear supernatant from the non-entrapped extract, the absorbance of the supernatant for the non-entrapped extract was measured at the appropriate max using a UV-visible spectrophotometer. Tricon-X100 solution was used to lyse the vesicles in the sediment before being diluted with the proper buffer and having absorbance measurements made at the proper max. The total amount of phytoconstituents in 1 ml of phytosomal dispersion was then calculated from the amount of phytoconstituents in the supernatant and sediment.^[59]

Drug content

By thoroughly dissolving a precisely weighed quantity of phytosomal dispersion in 10 ml of methanol, the drug concentration of the phytosomes was ascertained. After a reasonable

dilution, the absorbance was measured using spectroscopic techniques at an appropriate wavelength to estimate the drug concentration. [60]

Advantages of phytosome^[61]

- ➤ Herbal extracts' bioavailability has been increased as a result of complexation with phospholipids and enhanced intestinal gastric absorption.
- ➤ They facilitate improved absorption from the intestinal lumen by permeating the non-lipophilic herbal extract, which would not otherwise be able to pass the cell membrane.
- The components of phytosomes have also received approval for use in medicinal and cosmetic products, and the formulation is secure and efficient.
- ➤ Because they are simple to make and may quickly increase the bioavailability of phytoconstituents, phytosomes have been utilised to deliver hepatoprotective phytoconstituents. In addition, because phospholipid also has hepatoprotective action, this creates a synergistic effect for liver protection.
- When employed as active ingredients to protect the skin from exogenous or endogenous impacts in everyday as well as stressful environmental situations, phytosomal technology is affordable and offers a range of beneficial effects.
- They act as a conduit for the distribution of a wide range of medications (peptides, proteins, molecules).
- ➤ They can also be utilised for improved transdermal and dermal distribution of active ingredients through the skin, or vesicular systems, which are passive, non-invasive, and ready for rapid commercialization.
- An integral component of the cell membrane employed in phytosome technology, phospholipid serves as a transporter and nourishes the skin.
- ➤ Drug entrapment during formulation preparation is not a concern. Additionally, the entrapment efficiency is great and further specified due to the fact that the drug creates its own receptors after being conjugated with lipid.
- ➤ Due to the formation of chemical linkages between the phosphatidylcholine and phytoconstituents, they have a superior stability profile.

CONCLUSIONS

The usual method for obtaining turmeric's health benefits is through long-term, low-dose food ingestion. For turmeric to be used rationally in the treatment of human illnesses, a detailed understanding of the effective dosage, safety, and mechanism of action is necessary.

If turmeric is to be used for addressing human needs and enhancing human wellbeing, more clinical investigations are required. Antibacterial, antiviral, anti-inflammatory, anti-tumor, antioxidant, antiseptic, cardioprotective, hepatoprotective, nephroprotective, radioprotective, and digestive actions are only a few of turmeric's properties. Numerous substances, including curcumin, volatile oil, and curcuminoids, which have been discovered to have strong pharmacological activities, have been identified by phytochemical research of turmeric. This paper's thorough systematic evaluation demonstrates that curcumin lessens the negative effects of radiation or chemotherapy, which enhances patients' quality of life. Curcumin has been shown in several trials to prolong patient life and reduce tumour markers.

Acknowledgement

The conception and writing of this article were greatly assisted by all of the above authors.

Conflict of interest

The Authors declare no conflict of interest.

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