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Engineering technologies for curcumin recovery from *Curcuma longa* L.: Advances, process optimization, and phytomedicinal applications

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Abstract

The main bioactive substance derived from *Curcuma longa* L. rhizomes, curcumin, has garnered a lot of interest because of its many pharmacological characteristics and industrial uses. With an emphasis on curcumin's antioxidant, anti-inflammatory, antibacterial, anticancer, neuroprotective, and cardioprotective properties; this article offers a thorough summary of the phytomedicinal relevance of curcumin. Both traditional extraction methods, such as solvent and Soxhlet extraction, and cutting-edge engineering technologies, such as ultrasound-assisted extraction, microwave-assisted extraction, supercritical fluid extraction, enzyme-assisted extraction, and pressurised liquid extraction, are critically examined in this article. In order to increase extraction efficiency and environmental sustainability, recent developments in green extraction techniques specifically, the use of deep eutectic solvents and sustainable solvent systems are also covered. Important process optimisation techniques are also highlighted in the paper, such as the use of statistical tools like artificial neural networks and response surface approach to identify the best extraction parameters. A summary of curcumin's industrial uses in the food, cosmetic, pharmaceutical, and nutraceutical industries is also provided. The article concludes by outlining future research directions like hybrid extraction technologies, nanoencapsulation systems, green solvents, and artificial intelligence-based process optimisation. It also discusses the main obstacles to curcumin utilisation, such as low bioavailability, stability concerns, and challenges in large-scale implementation. All things considered, the review offers insightful information on the creation of effective and sustainable methods for curcumin extraction and use in a range of industrial applications.

1. Introduction

Traditional healthcare systems have relied heavily on medicinal plants for a long time, and these plants still play an important part in contemporary treatment approaches. Ayurveda, TCM, and the Unani systems are just a few of the many medicinal traditions that have long relied on chemicals produced from plants to cure and prevent illness (WHO, 2013; Ekor, 2014). Extensive scientific research on bioactive phytochemicals with potential pharmacological advantages has been conducted in recent decades due to the growing interest in natural and plant-based medicines (Rates, 2001; Newman and Cragg, 2020). Because of their reduced toxicity, better biocompatibility, and less undesirable side effects, natural chemicals originating from plants are often thought of as safer alternatives to manufactured pharmaceuticals (Ekor, 2014). Pharmaceutical, nutraceutical, functional food, and cosmeceutical uses for bioactive chemicals originating from plants are therefore receiving a lot of attention (Gul *et al.*, 2016).

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Curcumin, among these phytochemicals, has received a great deal of attention because of the promising medicinal effects it may have (Anand *et al.,* 2007; Hewlings and Kalman, 2017). Turmeric, or Curcuma longa, is a perennial plant in the Zingiberaceae family that is mostly harvested for its rhizomes (Prasad *et al.,* 2014). Medicinal, culinary, and as a natural dye, turmeric has a long history of usage (Aggarwal *et al.*, 2007). Curcumin is the most prevalent and physiologically active chemical among various curcuminoids found in the rhizomes of *Curcuma longa* (Prasad *et al.*, 2014). Because of its wide range of pharmacological effects and its uses in phytomedicine, curcumin, the compound that gives turmeric its distinctive brilliant yellow hue, has garnered a great deal of interest from scientists (Hewlings and Kalman, 2017).

The antioxidant, anti-inflammatory, antibacterial, anticancer, hepatoprotective, cardioprotective, neuroprotective, and immunomodulatory properties of curcumin have been shown in several studies (Anand *et al.,* 2007; Gupta *et al.,* 2013). Inflammation, oxidative stress, cell proliferation, and apoptosis are some of the biological processes that curcumin may modify, which is where its medicinal effects come from (Aggarwal and Sung, 2009). One example is that curcumin can reduce the expression of pro-inflammatory cytokines and enzymes including cyclooxygenase-2 (COX-2) and tumour necrosis factor-α (TNF-α), as well as inflammatory transcription factors like nuclear factor-γB (NF-κB) (Gupta *et al.*, 2013). Furthermore, curcumin has powerful antioxidant properties, since it scavenges ROS and boosts the efficiency of the body's own antioxidant enzymes (Hewlings and Kalman, 2017). The compound curcumin has been extensively studied in the pharmaceutical industry for its potential to treat a variety of long-term health issues, including cancer, heart disease, diabetes, neurological disorders, and inflammatory disorders (Anand *et al*., 2007; Hewlings and Kalman, 2017).

Curcumin has several uses beyond medicine, such as an antioxidant and natural food colourant (Gul *et al*., 2016). Curcumin is gaining more attention as a functional food component due to the increasing demand for natural ingredients and clean-label food items among consumers (Khan *et al*., 2019). Additionally, curcumin has become more significant in the nutraceutical industry, where it is frequently used in nutritional supplements with the goal of enhancing health and warding off illness (Hewlings and Kalman, 2017). There is a great need for effective extraction and purification methods that can produce high-quality curcumin on an industrial scale due to the rising demand for curcumin in the pharmaceutical, nutraceutical, and food sectors worldwide (Chemat *et al*., 2017).

The technological hurdles in extracting curcumin from turmeric rhizomes outweigh the compound's substantial economic and medical worth. Curcumin concentrations in turmeric are often low, comprising just 2-5% of the rhizome's dry weight, which is one of the main challenges (Prasad *et al*., 2014). In addition, curcumin has low water solubility and low stability in certain environments (Anand *et al*., 2007). Light, heat, oxygen, and acidic pH all has a negative effect on it (Wang *et al*., 1997). The compound's extraction and subsequent stabilisation during processing and storage are both made more difficult by these physicochemical features. Therefore, there has been a shift in emphasis in the scientific community toward finding ways to extract curcumin most effectively without compromising its bioactivity or structural integrity (Chemat *et al*., 2017).

According to Azmir *et al*. (2013), traditional methods for extracting curcumin include maceration, solvent extraction, and Soxhlet extraction. These procedures include dissolving the plant matrix containing curcuminoids in organic solvents and then isolating them. These methods have a number of serious drawbacks, despite their widespread use and relative simplicity. Extraction using traditional methods sometimes takes a long time, uses a lot of organic solvent, and uses a lot of energy (Azmir *et al*., 2013). Also, thermolabile compounds may degrade during extraction if heat is applied for too long, which lowers the curcumin yield and quality (Chemat *et al*., 2017). There has to be a shift toward more environmentally friendly extraction methods because of the problems caused by the widespread use of organic solvents.

In light of these constraints, there has been a concerted effort to improve curcumin extraction through the creation of cutting-edge technical solutions that are both efficient and environmentally friendly. Azmir *et al*. (2013) and Chemat *et al*. (2017) found that modern extraction techniques like ultrasound-assisted extraction, microwave-assisted extraction, supercritical fluid extraction, enzyme-assisted extraction, and pressurised liquid extraction are promising for improving turmeric curcumin recovery. To improve mass transfer, disturb plant cell architecture, and release intracellular bioactive chemicals, these technologies use novel physical and chemical processes. To illustrate, one method uses sonic cavitation to penetrate plant cell walls and enhance solvent penetration; another uses microwaves to speed up the extraction process (Chemat *et al*., 2017). Also, supercritical fluid extraction is an eco-friendly method that efficiently and selectively extracts non-polar phytochemicals like curcumin using supercritical carbon dioxide (Azmir *et al*., 2013).

Optimal methods for extracting phytochemicals have recently emerged, thanks in part to developments in food and biochemical engineering. By combining engineering concepts with extraction technologies, critical process parameters such solvent composition, temperature, pressure, and extraction time may be precisely controlled (Chemat *et al*., 2017). To find the best extraction conditions that maximise curcumin yield while minimising solvent usage and energy consumption, process optimisation techniques like artificial neural networks and statistical modelling approaches like response surface methodology are being used more and more (Bezerra *et al*., 2008).

The increasing focus on environmentally friendly chemistry and sustainable processing methods is another noteworthy development in the field of phytochemical extraction. By decreasing energy consumption, increasing process efficiency, and decreasing the use of harmful solvents, modern extraction technologies strive to minimise environmental effect (Chemat *et al*., 2017). There has been a lot of interest in developing eco-friendly solvent systems that can replace traditional organic solvents, such ionic liquids and deep eutectic solvents (Smith *et al*., 2014). To further enhance extraction performance and sustainability, researchers are investigating innovative technologies such high-pressure processing, pulsed electric field-assisted extraction, and hybrid extraction systems that combine various approaches (Barba *et al*., 2015).

By methodically evaluating traditional, advanced, and hybrid extraction strategies for curcumin recovery, this study offers a fresh, integrated viewpoint in contrast to other studies that mostly detail individual extraction techniques in isolation. This study presents a novel paradigm for the effective and sustainable extraction of curcumin by bringing together ideas of food engineering, green chemistry, and pharmacological relevance. Additionally, this study brings attention to newly developed hybrid extraction methods and process optimisation tools that have not been thoroughly examined in previous literature. New insights into the design of next-generation curcumin extraction systems are offered by this study, which critically evaluates extraction efficiency, scalability, environmental effect, and industrial application.

Developing effective and sustainable solutions for the recovery and processing of curcumin is vital, considering its expanding relevance in phytomedicine and the increasing demand for high-quality natural bioactive chemicals. Thus, this study takes an interdisciplinary approach by combining curcumin's food system applications, pharmacological significance, and food engineering technologies. New developments in extraction methods, optimisation strategies for processes, and environmentally friendly extraction practices are the main topics of this review. We also go over some of the possible consequences of these technologies for curcumin's industrial production and phytomedicinal uses. Curcumin is a significant bioactive ingredient, and this study aims to highlight future approaches for optimal recovery and utilisation by integrating information from food engineering, phytochemistry, and pharmaceutical sciences.

2. Botanical and phytochemical profile of turmeric

A perennial rhizomatous plant, turmeric is a member of the Zingiberaceae family that also contains ginger (*Zingiber officinale* Roscoe) and cardamom (*Elettaria cardamomum* L.), two other economically significant species (Prasad *et al*., 2014; Ravindran *et al*., 2007). Because it thrives in hot, humid conditions with rich, well-drained soil, this plant finds widespread cultivation in subtropical and tropical areas (Ravindran *et al*., 2007). The Indian subcontinent is said to be the birthplace of turmeric, a spice that has been farmed for millennia for its use in cooking and traditional medicine, especially in Ayurveda and TCM (Aggarwal *et al*., 2007).

Turmeric is grown all over the world, in places including Bangladesh, India, China, Indonesia, and Sri Lanka, as well as in several African and Central American nations (FAO, 2020). According to Chaudhary *et al*. (2018), India accounts for approximately 80% of the world's turmeric production, making it the leading producer, consumer, and exporter of the spice. The Indian states of Telangana, Andhra Pradesh, Tamil Nadu, Maharashtra, Karnataka, and Odisha are among the most important producers of turmeric (Chaudhary *et al*., 2018). Thanks to its enormous output and extensive application, turmeric has gained recognition as a valuable commercial spice crop and therapeutic plant in the herbal sector worldwide.

According to research by Prasad *et al*. (2014), the average height of *C. longa*, a herbaceous plant, is between 60 and 100 cm. According to Ravindran *et al*. (2007), the plant's subterranean rhizome gives birth to a pseudostem that is produced by the tightly wrapped leaf sheaths, which in turn produce big, oblong to lanceolate leaves. The 30-45 cm long leaves can be a brilliant green colour and include a strong midrib. The rhizome of turmeric plants sprouts thick spikes of flowers that range in colour from pale yellow to white (Ravindran *et al*., 2007). To keep its desired genetic features intact, this plant is mostly propagated vegetatively, utilising rhizome segments instead of seeds.

When it comes to medical and commercial value, the subterranean rhizome of the turmeric plant is unrivalled. The cylindrical, thick-branched rhizome is an organ for storing nutrients and bioactive chemicals (Prasad *et al*., 2014). Turmeric powder, made from boiling and dried rhizomes, has several use in the culinary, medicinal, and personal care sectors after harvest (Aggarwal *et al*., 2007). Hewlings and Kalman (2017) state that curcumin, one of the curcuminoids, is mainly responsible for turmeric powder's distinctive yellow-orange colour.

Turmeric rhizomes are chemically rich in a variety of bioactive chemicals, which give the spice its medicinal and practical uses. **(**Prasad *et al*.**,** 2014**)**. The major classes of phytochemicals present in turmeric include:

- **Curcuminoids:** The turmeric's colour and therapeutic qualities are caused by these main phenolic chemicals. Curcumin, demethoxy curcumin, and bisdemethoxy curcumin are the three primary curcuminoids (Prasad *et al*., 2014). According to Hewlings and Kalman (2017), curcumin stands out as the most prevalent and physiologically active molecule among them.
- **Essential oils:** The volatile oils found in turmeric rhizomes make about 3-7% of their dry weight. The sesquiterpenes and monoterpenes found in turmeric oils, including turmerone, atlantone, and zingiberene, are responsible for the spice's scent and some of its other medicinal uses (Ravindran *et al*.**,** 2007)**.**
- **Phenolic compounds**: Besides curcuminoids, turmeric contains other phenolic substances that exhibit antioxidant activity and contribute to its therapeutic potential **(**Gupta *et al*.**,** 2013**)**.
- **Terpenoids**: Various terpenoid compounds present in turmeric are responsible for its antimicrobial and anti-inflammatory properties **(**Gupta *et al*.**,** 2013**)**.
- **Polysaccharides**: The rhizomes of turmeric are said to contain bioactive polysaccharides that have anti-inflammatory and immunomodulatory properties (Prasad *et al*., 2014).

Curcuminoids are the most significant bioactive compounds among these phytochemical categories. Turmeric rhizomes usually contain 2-5% curcuminoids by dry weight; however, this percentage can change based on a number of variables such as cultivar, region of origin, growing circumstances, harvest timing, and processing techniques used after harvest (Prasad *et al*., 2014). Hewlings and Kalman (2017) found that curcumin makes up around 70-80% of the curcuminoid concentration, with demethoxy curcumin and bisdemethoxy curcumin making up lower amounts.

Traditional medicine and contemporary pharmacology both make use of turmeric rhizomes, which have a complex phytochemical makeup (Aggarwal *et al*., 2007). Gupta *et al*. (2013) found that curcuminoids are not the only phenolic chemicals and essential oils that provide turmeric its medicinal potential. These compounds work together to provide synergistic biological effects, including antioxidant, anti-inflammatory, antibacterial, and anticancer actions. Curcumin and other bioactive components in turmeric have attracted a lot of attention from scientists due to their desirable features, which have prompted the development of cutting-edge engineering techniques for their extraction and purification (Chemat *et al*., 2017).

The need of optimising growing practices, harvesting procedures, and extraction processes to guarantee optimal recovery of important bioactive compounds is further underscored by the heterogeneity in phytochemical content among various turmeric cultivars (Chaudhary *et al*., 2018). To improve the industrial use of turmeric-derived phytochemicals in culinary, medicinal, and nutraceutical applications, it is vital to understand the botanical properties and chemical composition of *C. longa*. This will allow for the development of effective extraction processes.

2.2 Chemical structure and physicochemical properties of curcumin

A member of the diarylheptanoids class of naturally occurring polyphenolic chemicals, curcumin is the primary bioactive component found in *C. longa* rhizomes (Anand *et al*., 2007; Priyadarsini, 2014). Because of its unusual molecular structure, which consists of two aromatic rings that have been substituted and linked by a seven-carbon linker chain, curcumin is chemically defined as 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione. The physicochemical characteristics and biological activities of curcumin are greatly affected by the presence of conjugated double bonds and β-diketone functional groups in this central linker (Priyadarsini, 2014).

The molecular structure is made up of two phenolic rings that have hydroxyl (-OH) and methoxy (-OCH_2) groups attached to them. According to Priyadarsini (2014), curcumin's powerful antioxidant capabilities are mostly due to its phenolic groups, which may donate hydrogen atoms to neutralise free radicals and reactive oxygen species. Conjugated double bonds give structural stiffness and enable electron delocalisation across the molecule; they are located in the middle seven-carbon chain, which is also called the heptadienedione bridge. Anand *et al.* (2007) found that curcumin's vivid yellow colour and significant absorption in the visible spectrum are caused by its vast conjugation system.

Curcumin has a molecular weight of 368.38 g/mol and is chemically described as $C_{21}H_{20}O_6$. The presence of aromatic rings and conjugated carbon chains gives the molecule a relatively hydrophobic character, limiting its solubility in water (Anand *et al.*, 2007). As a result, curcumin has extremely low water solubility, usually only dissolving in a few micrograms/ml under physiological circumstances. Oral administration results in limited bioavailability, which is partially caused by its weak water solubility.

Curcumin, on the other hand, dissolves easily in several organic solvents, including chloroform, acetone, dimethyl sulfoxide, ethanol, and methanol (Chemat *et al.*, 2017). Organic solvents increase curcumin's solubility because the solvent molecules form favourable interactions with the nonpolar portions of the curcumin molecule. When trying to extract curcumin from turmeric rhizomes, this quality is crucial since organic solvents work so well in this procedure. Researchers are looking at greener alternatives to organic solvents for curcumin extraction, including supercritical fluids, ionic liquids, and deep eutectic solvents, because of the environmental and safety problems associated with their usage.

One further thing that makes curcumin special is that it may exist in two different tautomeric forms: enol and keto. According to Priyadarsini (2014), the formation of tautomerism is caused by the intramolecular proton transfer that can occur when the â-diketone moiety is present in the central chain. Two carbonyl groups are present in the keto form of the molecule; however, one of these groups is transformed into an enol group by means of hydrogen migration and reorganisation of the double bonds in the enol form.

The environment has a significant impact on how stable these tautomeric forms are. The enol form is often more stable and predominates in organic solvents and alkaline environments because of the establishment of intramolecular hydrogen bonds and resonance stabilisation (Wang *et al.*, 1997). Since the enol form allows electron donation and radical scavenging methods, it makes a substantial contribution to curcumin's antioxidant action. On the other hand, the keto form is more common in acidic and neutral water. Thus, curcumin's chemical reactivity, stability, and biological activity are heavily influenced by the keto-enol equilibrium.

Climate, temperature, light, and oxygen availability are some of the environmental variables that have a significant impact on curcumin's stability. In acidic situations, curcumin remains quite intact, while in alkaline ones, it degrades quickly. Curcumin may break down into smaller phenolic compounds including ferulic acid, vanillin, and feruloylmethane when exposed to an acidic pH. The curcumin's stability throughout processing, storage, and formulation is greatly impacted by these mechanisms of degradation. Furthermore, curcumin is photodegradation sensitive, which means that it might lose its bioactivity and structural integrity after being exposed to light for an extended period of time.

The hydrophobicity, chemical instability, and poor water solubility of curcumin are some of its physicochemical features that make its extraction, formulation, and therapeutic use very difficult (Anand *et al.*, 2007). Due to these drawbacks, a great deal of effort has gone into developing new technical methods to increase curcumin's bioavailability and stability (Gupta *et al.*, 2013). To make curcumin more bioavailable and stable, scientists have come up with many strategies, such encapsulation, nanoemulsion creation, liposomal delivery methods, and nanoparticles made of polymers.

It is crucial to comprehend curcumin's molecular structure and physicochemical properties in order to develop effective methods of extraction and formulation (Chemat *et al.*, 2017). The recovery efficiency, purity, and functional characteristics of the extracted substance are greatly affected by the interaction between curcumin's chemical structure and the circumstances of extraction. Therefore, understanding these physical and chemical properties lays the groundwork for creating cutting-edge technical tools to efficiently extract and use curcumin in pharmaceutical, nutraceutical, and functional food uses.

3. Phytomedicinal significance of curcumin

Anand *et al.* (2007) and Hewlings and Kalman (2017) note that curcumin, the main curcuminoid extracted from *C. longa* rhizomes, has garnered a lot of interest in the last few decades because of its wide range of pharmacological actions and therapeutic possibilities. Inflammation, oxidative stress, cell proliferation, and apoptosis are all impacted by curcumin, a polyphenolic substance that occurs naturally (Gupta *et al.*, 2013). In contrast to many traditional medications, curcumin acts on many molecular pathways simultaneously. Curcumin has thus far been the subject of substantial research as a potential phytomedicinal agent for the treatment and prevention of a wide range of chronic diseases, such as cancer, heart disease, diabetes, neurological disorders, and inflammatory disorders (Aggarwal and Sung, 2009; Gupta *et al.*, 2013).

One of curcumin's main pharmacological effects is the way it controls the expression of genes and enzymes linked to disease development by influencing intracellular signalling pathways (Gupta *et al.*, 2013). According to Aggarwal and Sung (2009), curcumin has the ability to affect several proteins that are essential for maintaining cellular homeostasis, including growth factors, transcription factors, protein kinases, and inflammatory mediators. Researchers in the domains of phytomedicine, nutraceuticals, and functional foods have been studying curcumin extensively because of its many biological actions. Below, we will go over the main medicinal benefits of curcumin.

3.1 Antioxidant activity

Hewlings and Kalman (2017) found that oxidative stress has a significant role in the development of several long-term health problems. These include cancer, heart disease, diabetes, and neurological disorders. According to Gupta *et al.* (2013), oxidative stress happens when the amount of reactive oxygen species (ROS) produced by a system is out of sync with its antioxidant defences capacity to neutralise these molecules. Lipides, proteins, and DNA are all vulnerable to ROS damage, which can cause cells to malfunction and diseases to emerge.

Because of its conjugated double-bond structure and phenolic hydroxyl groups, curcumin is able to scavenge free radicals and display significant antioxidant activity (Priyadarsini, 2014). Superoxide anions, hydroxyl radicals, hydrogen peroxide, and reactive nitrogen species are among the reactive species that the molecule may neutralise (Gupta *et al*., 2013). In addition to its free radical scavenging effects, curcumin boosts the efficiency of the body's own antioxidant enzymes. The cellular redox equilibrium is maintained by enzymes such as glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT) (Hewlings and Kalman, 2017).

In addition, research has demonstrated that curcumin can activate the Nrf2 signalling pathway, which controls the production of several detoxifying and antioxidant enzymes. In addition to curcumin's preventive benefits in a number of diseases, activation of this pathway strengthens cellular defence systems against oxidative stress (Balogun *et al*., 2003).

3.2 Anti-inflammatory activity

The immune system's intricate reaction to pathogens, injuries, or other potentially dangerous stimuli is known as inflammation (Aggarwal and Sung, 2009). Arthritis, cardiovascular disease, inflammatory bowel disease, and neurological illnesses are just a few of the many conditions that can arise as a result of chronic inflammation, in contrast to the beneficial effects of acute inflammation. Gupta *et al*. (2013) noted that curcumin has been extensively studied for its potential as a natural anti-inflammatory drug due to its powerful anti-inflammatory characteristics. Modulating important signalling pathways involved in the inflammatory response is the primary mechanism by which the chemical exerts its anti-inflammatory actions. Curcumin affects the expression of several inflammatory genes *via* targeting the nuclear transcription factor NF-κB, which is one of its most significant targets. According to Aggarwal and Sung (2009) and Gupta *et al*. (2013), curcumin decreases the production of pro-inflammatory mediators such TNF-α, IL-1β, IL-6, and COX-2 *via* blocking the activation of NF-κB.

Further, research has shown that curcumin can decrease the activity of certain inflammatory enzymes, such as LOX and iNOS (Chainani-Wu, 2003). Curcumin protects tissues from inflammatory damage and efficiently lowers inflammatory responses through these methods.

3.3 Anticancer properties

The hunt for safer and more effective anticancer drugs has heated up in recent years, as cancer remains a top killer globally (Anand *et al*., 2007). Because of its effects on many molecular pathways involved in tumour growth and progression, curcumin has gained attention as a potential anticancer drug (Gupta *et al*., 2013). Several pathways are responsible for curcumin's anticancer properties. The elimination of defective or aberrant cells is facilitated by inducing apoptosis, a process of planned cell death. According to Anand *et al*. (2007), curcumin hinders Bcl-2 and other anti-apoptotic proteins while activating apoptotic pathways via controlling the production of pro-apoptotic proteins including Bax and caspases. The eradication of cancer cells is facilitated by this control.

Inhibiting cell growth is another significant anticancer action of curcumin. By influencing cyclins and cyclin-dependent kinases, curcumin disrupts the course of the cell cycle and stops unchecked cell division (Gupta *et al*., 2013). In addition, research has demonstrated that curcumin inhibits angiogenesis, the process by which tumours receive oxygen and nutrition through the development of new blood vessels. According to Aggarwal and Sung (2009), curcumin limits tumour development and metastasis by blocking angiogenic factors including vascular endothelial growth factor (VEFG). According to Gupta *et al*. (2013), curcumin can hinder tumour invasion and metastasis by regulating proteins involved in the breakdown of the extracellular matrix, such as matrix metalloproteinases. Curcumin is a potential option for cancer prevention and adjuvant therapy because to these coupled processes.

3.4 Antimicrobial activity

Gupta *et al*. (2013) found that curcumin has strong antibacterial properties against several pathogenic microbes, such as viruses, fungi, and bacteria. One explanation for curcumin's antibacterial effects is that it can damage microbial cell membranes and impair their metabolic activities. Tyagi *et al*. (2015) found that curcumin inhibits the growth of both Gram-positive and Gram-negative bacteria, including Salmonella, Staphylococcus aureus, and Escherichia coli. Because it damages bacterial cell membranes, changes membrane permeability, and disturbs cellular homeostasis, the chemical can impede bacterial growth.

By preventing the expansion of fungal cells and disrupting their ability to maintain their membrane integrity, curcumin demonstrates antifungal efficacy against species like Candida albicans (Martins *et al*., 2009). Curcumin has also been found to have antiviral effects against many viruses, according to research (Moghadamtousi *et al*., 2014). These effects are thought to work by blocking the reproduction of the virus or interfering with its ability to make proteins. Thanks to its antibacterial qualities, curcumin might be used to create natural antimicrobial agents that can be used for food and pharmaceutical preservation.

3.5 Neuroprotective and cardioprotective effects

A possible treatment for neurological and cardiovascular diseases, curcumin has demonstrated encouraging neuroprotective and cardioprotective benefits (Hewlings and Kalman, 2017). Neuronal degeneration is a hallmark of inflammatory and oxidative stress-related neurological disorders including Parkinson's and Alzheimer's. Gupta *et al*. (2013) found that curcumin can decrease oxidative stress in neural tissues by increasing antioxidant defences and scavenging reactive oxygen species. Also, according to Ringman *et al*. (2005), curcumin can prevent the buildup of Alzheimer's disease-related amyloid-beta proteins. Curcumin may help prevent neuronal degeneration and enhance cognitive function via various pathways.

Research has shown that curcumin can have positive effects on the cardiovascular system, including better endothelial function, reduced lipid peroxidation, and lower levels of inflammatory markers linked to cardiovascular illnesses (Panahi *et al*., 2016). The oxidation of low-density lipoproteins (LDL) is a key component in the development of atherosclerosis; curcumin can assist control cholesterol metabolism and prevent this (Hewlings and Kalman, 2017). Curcumin may have a role in lowering the risk of cardiovascular illnesses such hypertension, coronary artery disease, and heart failure due to its cardioprotective properties.

4. Conventional methods for curcumin extraction

Using organic solvents and lengthy extraction procedures, traditional methods have been used to obtain curcumin from *C. longa* rhizomes (Azmir *et al*., 2013; Chemat *et al*., 2017). Because of their ease of use and low equipment requirements, these approaches have found extensive application in labs and small-scale companies. Traditional methods have a number of limitations, though, including the potential destruction of thermolabile chemicals, lengthy extraction durations, insufficient selectivity, and excessive solvent consumption (Azmir *et al*., 2013).

It is common practice to pre-treat plant material, extract solvents, and then purify curcumin (Sasidharan *et al*., 2011). In order to maximise the surface area that may interact with the solvent, the turmeric rhizomes are first washed, dried, and crushed into a fine powder. The curcuminoids are extracted from the plant matrix by subjecting the powdered material to solvent-based extraction techniques. Although these methods are widely used, they are slowly being supplanted by more modern engineering technologies due to their low extraction efficiency (Chemat *et al*., 2017).The process for extraction of curcumin is shown in Figure 1.

Turmeric rhizome
↓
Drying and grinding
↓
Pre-treatment
↓
Extraction method
↓
Filtration
↓
Solvent removal
↓
Purification
↓
Curcumin extract

Figure 1: Curcumin extraction process flowchart.

4.1 Solvent extraction

According to Azmir *et al*. (2013), curcumin may be extracted from turmeric rhizomes via solvent extraction, which is a commonly used traditional approach. Here, organic solvents like ethanol, methanol, acetone, ethyl acetate, or hexane are used to soak or combine the powdered turmeric material. According to Sasidharan *et al*. (2011), the curcuminoids found in the plant matrix can be dissolved by these solvents by mass transfer and diffusion. Many variables affect how well solvent extraction works, such as the polarity of the solvent, the temperature at which it is carried out, the length of time it takes to complete the process, the size of the plant material's particles, and the ratio of solvent to solid (Azmir *et al*., 2013). Curcumin has a greater solubility in organic solvents as opposed to water since it is a hydrophobic and somewhat nonpolar molecule (Anand *et al*., 2007). Many people choose acetone and ethanol over other organic solvents due to their low toxicity and great extraction efficiency (Chemat *et al*., 2017). In order to extract bioactive chemicals from plants, a solvent must first permeate their tissues and cells. Parts of the plant cells with a greater concentration diffuse to parts of the solvent medium with a lower concentration. Extracts high in curcumin are obtained by first filtering out plant residues and then concentrating them by evaporation (Sasidharan *et al*., 2011).

Despite solvent extraction's widespread use, it has a number of serious drawbacks that make it less than ideal. The total recovery of curcuminoids requires a lengthy extraction process, which can take many hours to even days depending on the circumstances (Azmir *et al*., 2013). This is a major downside. The use of organic solvents in large quantities also increases operational expenses and has an adverse effect on the environment (Chemat *et al*., 2017). It is also possible for curcumin to undergo partial degradation when subjected to high temperatures during solvent evaporation, which would lower its biological activity and total yield (Wang *et al*., 1997). The fact that solvent extraction is easy to scale up for large output and needs relatively basic equipment means that it is still utilised in many industrial processes despite these shortcomings.

4.2 Soxhlet extraction

According to Azmir *et al*. (2013), another popular traditional method for obtaining curcumin from turmeric rhizomes is soxhlet extraction. This technique is a continuous extraction procedure because it efficiently extracts target components by cycling the solvent through the plant material repeatedly. Soxhlet extraction involves placing the turmeric powder sample within a cellulose or filter paper porous thimble. The thimble is thereafter immersed in a hot solvent and rinsed repeatedly in the Soxhlet device. A distillation flask is used to heat the solvent until it evaporates and flows upward into a condenser. When the solvent condenses, it falls down onto the plant matter in the extraction chamber. The solvent will immediately return to the boiling flask as soon as the chamber is filled with it, bringing the dissolved curcuminoids along for the ride. The extraction procedure is carried out by repeatedly doing this cycle (Sasidharan *et al*., 2011).

Soxhlet extraction has the potential to obtain higher extraction yields than basic maceration methods, which is a benefit (Azmir *et al*., 2013). An improved method for extracting curcuminoids is continuous solvent recycling, which involves continually interacting with plant material with new solvent. Also, once the equipment is set up, Soxhlet extraction requires little to no human interaction, which makes it ideal for extraction procedures on a laboratory size. Nevertheless, there are a number of major drawbacks to this approach as well. Extraction *via* Soxhlet usually takes a long time and a lot of heat, anything from 6-24 h (Azmir *et al*., 2013). Curcumin and other chemicals that are sensitive to heat can degrade when exposed to heat over long periods of time (Wang *et al*., 1997). Chemical *et al*. (2017) also noted that the method uses a lot of organic solvents, which might be harmful to the environment and people's health. Continuous heating also raises operational expenses due to its high energy need. Alternative extraction procedures that provide better efficiency, less solvent usage, and more environmental sustainability have been widely investigated by researchers due to these restrictions. (Chemat *et al*., 2017).

5. Emerging engineering technologies for curcumin extraction

In recent years, the limitations associated with conventional extraction methods have led to the development of advanced engineering technologies designed to improve the recovery of curcumin from turmeric (Chemat *et al.*, 2017; Azmir *et al.*, 2013). These modern extraction techniques aim to enhance extraction efficiency, reduce processing time, minimize solvent consumption, and preserve the bioactivity of curcumin (Chemat *et al.*, 2017). Many of these technologies rely on innovative physical and chemical mechanisms to disrupt plant cell structures and facilitate the release of intracellular compounds (Azmir *et al.*, 2013).

5.1 Ultrasound assisted extraction (UAE)

Chemat *et al*. (2017) noted that among the most promising methods for recovering bioactive chemicals from plant materials, ultrasound aided extraction stands out. According to Vilkhu *et al*. (2008), this technique improves extraction by using high-frequency ultrasonic waves, usually between 20 and 100 kHz. In ultrasound-assisted extraction, acoustic cavitation-the process of creating, expanding, and violently collapsing tiny bubbles in a solvent-is the underlying mechanism (Chemat *et al*., 2017). Mechanical rupture of cell walls occurs when these bubbles burst close to plant tissues, creating areas of localised high heat and pressure. Intracellular chemicals, including curcumin, are released into the surrounding solvent as a result of this disturbance.

The use of ultrasonic waves has several benefits for plant materials, including the breakdown of cell walls, improved solvent penetration, and increased mass transfer rates (Vilkhu *et al*., 2008). Because of these effects, the extraction process is accelerated and target chemicals are recovered more efficiently. Reducing extraction time, lowering solvent consumption, improving extraction efficiency, and better preserving thermolabile chemicals are some of the advantages of ultrasound-assisted extraction over conventional solvent extraction methods (Chemat *et al*., 2017). Research has shown that with the help of ultrasound, the extraction of curcumin may be done more faster, cutting down the processing time from hours to minutes (Azmir *et al*., 2013). In addition to being easily scalable for industrial purposes, the technology is also easy to apply.

5.2 Microwave assisted extraction (MAE)

Another cutting-edge method that has recently attracted a lot of interest for the extraction of bioactive chemicals from plant materials is microwave aided extraction (Azmir *et al*., 2013). To improve extraction, this technique uses microwaves to quickly heat the plant tissues and solvent (Chan *et al*., 2011). The fast oscillation and friction caused by the interaction of microwave radiation with polar molecules in the solvent and plant tissues create heat. According to Chan *et al*. (2011), when plant cells are heated quickly, the internal pressure rises, leading to the eventual rupture of the cell wall and the release of intracellular chemicals like curcumin.

Reducing extraction time compared to conventional procedures is one of the key benefits of microwave-assisted extraction (Azmir *et al*., 2013). Extractions using conventional solvents might take hours, while those using microwaves can get the same or better results in only a few minutes. Microwave extraction also offers better energy efficiency and often uses less solvent (Chemat *et al*., 2017). Improved product quality, reduced processing times, and increased extraction selectivity are some of the additional advantages of microwave aided extraction. Microwave assisted extraction also helps to preserve bioactive chemicals. Because of this, microwave technology has grown in popularity for use in extraction procedures on a large and small scale in both laboratories and factories.

5.3 Supercritical fluid extraction (SFE)

According to several studies (Azmir *et al*., 2013; Chemat *et al*., 2017), supercritical fluid extraction is a very effective and ecologically safe way to extract phytochemicals from plant materials. Fluids that are kept at temperatures and pressures over their critical points can display gaseous and liquid characteristics in this method. Supercritical carbon dioxide is most often employed since it is harmless to humans, fire, and the environment (Reverchon and De Marco, 2006). Supercritical CO_2 has a low viscosity and a high diffusivity, making it ideal for dissolving curcumin and other nonpolar chemicals found in plant matrices. According to Reverchon and De Marco (2006), one major benefit of supercritical CO_2 extraction is that it may selectively extract certain molecules by manipulating process variables like temperature and pressure. Curcumin may be made much more soluble and extracted more efficiently with the use of modest quantities of co-solvents, most often ethanol.

Supercritical fluid extraction has a number of advantages over more traditional extraction techniques, such as greater product purity, less solvent residue, and more extraction selectivity (Azmir *et al*., 2013). In addition, this method is more eco-friendly as carbon dioxide is used instead of harmful chemical solvents (Chemat *et al*., 2017).

5.4 Enzyme assisted extraction

According to Puri *et al*. (2012), one biotechnological method for enhancing the recovery of bioactive chemicals from plant materials is enzyme aided extraction. This method breaks down plant cell wall components using enzymes including cellulase, pectinase, and hemicellulase. The primary components of plant cell walls-cellulose, hemicellulose, and pectin-serve as barriers that regulate the efflux of chemicals within the cell. Enzymes aid in the extraction of curcumin and other phytochemicals by breaking down these structural components (Puri *et al*., 2012). Plant materials with abundant polysaccharides and fibrous structures are ideal candidates for enzyme-assisted extraction. According to Azmir *et al*. (2013), the method is able to maintain curcumin's stability and bioactivity by operating at very mild circumstances.

5.5 Pressurized liquid extraction

The extraction of bioactive chemicals is enhanced using a state-of-the-art method called accelerated solvent extraction or pressurised liquid extraction, which makes use of high temperatures and pressure (Mustafa and Turner, 2011). The solvent can be heated past its boiling point without losing its liquid state when subjected to high pressure. According to Mustafa and Turner (2011), by combining high temperature and pressure, the solubility of curcumin is enhanced and the solvent is able to penetrate plant tissues more effectively. When compared to traditional solvent extraction procedures, these features greatly shorten extraction times while also improving mass transfer rates. Azmir *et al*. (2013) listed a number of benefits of pressurised liquid extraction, including less solvent use, more extraction efficiency, and faster processing times. Plus, it is automatable, therefore it is great for industrial applications that require high-throughput extraction. Table 1 shows the results of a comparison of several extraction techniques.

Table 1: Comparative analysis of different extraction methods

Method	Time	Solvent use	Yield	Environmental impact
Soxhlet	High	High	Moderate	Poor
UAE	Low	Moderate	High	Good
MAE	Very Low	Low	High	Good
SFE	Moderate	Very Low	Very High	Excellent

6. Green solvents and novel extraction approaches

Chemat *et al*. (2012) and Dai *et al*. (2013) note that researchers have been working on green extraction techniques to recover bioactive chemicals from plant materials due to rising environmental concerns and the desire for sustainable processing technologies. Organic solvents including hexane, methanol, and acetone are commonly used in conventional extraction processes, but they may be harmful to the environment and human health in excessive quantities (Azmir *et al*., 2013). Green extraction methods, on the other hand, keep extraction efficiency high while reducing solvent consumption, energy needs, and the use of solvents that are harmful to the environment (Chemat *et al*., 2012).

Environmentally friendly extraction practices adhere to a number of guiding principles, such as utilising renewable solvents, decreasing energy usage, increasing extraction efficiency, and minimising waste (Chemat *et al*., 2012). Due to their potential to improve curcumin recovery while lowering environmental impact, green solvents and new extraction techniques have garnered substantial attention in the context of curcumin extraction from *C. longa* rhizomes (Dai *et al*., 2013). Emerging technologies such as ionic liquids, deep eutectic solvents (DES), and natural deep eutectic solvents (NADES) hold great potential as environmentally friendly substitutes for traditional organic solvents. (Paiva *et al*., 2014).

6.1 Deep eutectic solvents (DES)

An emerging category of environmentally friendly solvents, deep eutectic solvents have recently attracted a lot of interest for phytochemical extraction from plants (Smith *et al*., 2014). A eutectic mixture with a melting point considerably lower than that of the individual components is generated when two or more components, usually a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA), combine through hydrogen bonding to form DES (Paiva *et al*., 2014). Sugars, organic acids, glycerol, choline chloride, and urea are some of the most common ingredients utilised to make DES. The stable liquid systems formed by these substances when mixed in the right molar ratios have distinctive physicochemical characteristics, making them ideal for phytochemical extraction.

A variety of bioactive chemicals, such as polyphenols, alkaloids, flavonoids, and curcuminoids, are very well soluble in deep eutectic solvents, which is a big plus (Dai *et al*., 2013). Curcumin is more easily dissolved from the plant matrix due to the strong hydrogen-bonding interactions between the solvent components and phytochemicals. Furthermore, DES are safer than traditional organic solvents because to their low volatility, low toxicity, and good thermal stability (Paiva *et al*., 2014).

The ability to adjust the characteristics of DES is another significant benefit. Changing the molar ratios of different types of hydrogen bond donors and acceptors allows researchers to vary the solvent system's polarity, viscosity, and extraction efficiency (Smith *et al*., 2014). Because of this adaptability, DES formulations may be fine-tuned for the extraction of bioactive chemicals like curcumin. Dai *et al*. (2013) found that curcumin production can be greatly improved using DES-based extraction techniques compared to standard solvents like ethanol or methanol. Reportedly, DES can be even more effectively extracted by combining it with sophisticated extraction methods like ultrasound- or microwave-assisted extraction, which improve mass transfer and cell wall breakdown. (Chemat *et al*., 2017).

6.2 Natural deep eutectic solvents (NADES)

Sugars, amino acids, organic acids, and organic bases are the only components of natural deep eutectic solvents, a kind of DES (Dai *et al*., 2013). The components of these solvents are usually recognised as safe, which makes them very appealing for usage in food and pharmaceutical applications. NADES are thought to imitate the natural solvent systems found in plant cells and have an impressive capacity to dissolve plant compounds (Dai *et al*., 2013). Because of this quality, bioactive substances may be efficiently extracted without sacrificing their stability or biological activity. Results from curcumin extraction using NADES formulations including choline chloride, citric acid, glucose, or glycerol have been encouraging (Paiva *et al*., 2014). The use of these solvents improves the extraction process's sustainability by increasing efficiency and decreasing the requirement for harmful organic solvents.

6.3 Ionic liquids in curcumin extraction

Welton (1999) noted that ionic liquids are another type of environmentally friendly solvents that have been investigated for phytochemical extraction. These ion-only solvents stay liquid at low temperatures and are completely non-reactive. Unique physicochemical qualities of ionic liquids include strong thermal stability, great solvating ability, and minimal vapour pressure. Ionic solutions have the ability to break down plant cell walls and improve the solubility of bioactive chemicals during phytochemical extraction procedures (Ventura *et al*., 2017). Using ionic liquids in conjunction with ultrasonic or microwave extraction methods has been shown to boost curcumin extraction yields in many experiments (Ventura *et al*., 2017). Concerns about their expensive cost and possible toxicity have restricted the large-scale commercial adoption of ionic liquids, despite their benefits (Welton, 1999). Therefore, it is generally believed that sustainable extraction procedures are better suited to using natural deep eutectic solvents.

6.4 Significance of green solvent extraction

There are various benefits to using environmentally friendly solvents like DES and NADES instead of more traditional extraction methods. Less pollution, more efficient extraction, and safer operations for everyone involved are just a few of the benefits (Chemat *et al*., 2012). Along with green chemistry and sustainable food processing, which prioritise eco-friendly manufacturing practices, green extraction technologies are in line with these ideals. Chemat *et al.* (2017) noted that new prospects have emerged for the development of efficient and sustainable phytochemical recovery procedures in the context of curcumin extraction, thanks to the integration of green solvents with current extraction technologies as ultrasound, microwave, or pressurised liquid extraction. The importance of green solvent extraction in the mass manufacturing of bioactive chemicals like curcumin for uses in pharmaceuticals, nutraceuticals, and functional foods is predicted to grow as this area of study develops further.

7. Process optimization strategies

According to Azmir *et al*. (2013) and Chemat *et al*. (2017), optimising various processing parameters is crucial for the efficient extraction of curcumin from plant sources. According to Bezerra *et al*. (2008), optimising the method is crucial for achieving the following goals: increasing curcumin production, decreasing solvent use, shortening processing time, and maintaining bioactive compound stability. Extraction conditions must be meticulously regulated to avoid degradation and maximise recovery of curcumin, which is sensitive to environmental variables such light, pH, and temperature (Wang *et al*., 1997). Finding the optimal extraction parameters to maximise curcumin recovery from *C. longa* rhizomes is the primary goal of optimisation methodologies (Azmir *et al*., 2013). The physical and chemical parameters that affect the release of curcuminoids from plant matrix in commercial and laboratory extraction methods are many. Since these characteristics are interrelated, adjusting any one of them could have a major impact on the extraction efficiency as a whole (Bezerra *et al*., 2008). Statistical and computational optimisation methods enable researchers to evaluate several variables and their interactions simultaneously, which is useful for methodically finding optimal circumstances (Bas and Boyacý, 2007).

7.1 Key parameters influencing extraction efficiency

7.1.1 Solvent type and concentration

Since the solubility of curcuminoids differs according to the polarity of the solvent, the selection of the solvent is crucial during curcumin extraction (Azmir *et al*., 2013). One example of a hydrophobic polyphenolic molecule is curcumin, which, according to Anand *et al.* (2007), is more soluble in organic solvents than water. Ethyl acetate, acetone, methanol, ethanol, and methanol are solvents that are frequently utilised in extraction operations. The extraction efficiency is also impacted by the solvent concentration. Solubility and polarity can be best achieved, for example, in aqueous ethanol solutions, which are widely utilised (Chemat *et al*., 2017). While certain phytochemicals are more easily extracted with more polar solvents, curcumin's solubility may be negatively affected by solvents with too much polarity. For this reason, optimising yield relies heavily on choosing the right solvent composition.

7.1.2 Extraction temperature

According to Azmir *et al*. (2013), the extraction rate is greatly affected by temperature, which has an effect on mass transfer and the solubility of curcumin in the solvent. Solvent penetration into plant tissues is improved and diffusion rates are increased at higher temperatures, leading to better intracellular chemical release. The breakdown of heat-sensitive chemicals, like curcumin, can occur at very high temperatures, though (Wang *et al*., 1997). So, to have good extraction efficiency without ruining the compound stability, you need keep the temperature at the sweet spot. For instance, according to Mustafa and Turner (2011), one method that uses increased temperatures to speed up the extraction process while decreasing processing time is pressurised liquid extraction and microwave-assisted methods. However, in order to avoid thermal degradation, the temperature needs to be properly regulated.

7.1.3 Extraction time

The amount of curcumin that can diffuse into the solvent from the plant matrix is dependent on the extraction time (Azmir *et al*., 2013). Since the solvent needs more time to permeate plant tissues and dissolve intracellular components, a longer extraction period usually results in a higher curcumin yield. On the other hand, Chemat *et al.* (2017) noted that curcumin degradation, higher operational expenses, and increased energy usage could result from extraction durations that are too long. As a result, getting the right amount of time to extract is crucial for effective recovery without sacrificing product quality. When compared to more traditional procedures, cutting-edge extraction techniques like ultrasound- and microwave-assisted extraction drastically shorten the extraction time (Vilkhu *et al*., 2008).

7.1.4 Particle size of plant material

According to Azmir *et al*. (2013), the size of the turmeric powder's particles is another crucial factor that influences the effectiveness of the extraction process. The surface area accessible for solvent interaction is increased by grinding the rhizomes into smaller particles, which improves the diffusion of curcumin into the solvent. Particles of a smaller size are able to penetrate the plant matrix more effectively, which in turn increases extraction efficiency. Problems with solvent separation and filtering system clogging are two examples of operational concerns that could arise from particles that are too tiny. Thus, in order to strike a balance between extraction efficiency and process practicality, it is necessary to determine an ideal particle size.

7.1.5 Solid to solvent ratio

The extraction process is also greatly affected by the plant material to solvent volume ratio (Azmir *et al*., 2013). The extraction efficiency is often enhanced by increasing the solvent volume, which in turn enhances the concentration gradient between the plant matrix and the solvent. The mass transfer and extraction yield are both enhanced when there is a higher solid-to-solvent ratio because there is more solvent available to dissolve the curcumin. Nevertheless, solvent recovery can become more complicated and processing costs can rise if solvent quantities are used in excess. In order to accomplish efficient extraction with minimal solvent usage, it is vital to optimise this parameter.

7.2 Statistical optimization techniques

Due to the complex interactions among extraction variables, traditional one-factor-at-a-time experiments are often insufficient for identifying optimal extraction conditions (Bas and Boyaci, 2007). Instead, modern studies employ statistical optimization techniques that allow simultaneous evaluation of multiple variables.

7.2.1 Response surface methodology (RSM)

According to Bezerra *et al*. (2008), response surface methodology (RSM) is a popular statistical approach for optimising processes in food engineering and phytochemical extraction. Here, curcumin yield is the response variable, and RSM employs mathematical and statistical models to assess the correlations between a number of independent variables. The central composite design (CCD) and the Box-Behnken design (BBD) are two examples of specific experimental designs that are used in this strategy (Bas and Boyacý, 2007). In order to understand how different parameters affect extraction efficiency, polynomial equations are generated from the experimental data.

The main advantages of RSM include:

- Reduction in the number of experimental trials
- Identification of interactions between variables
- Determination of optimal process conditions
- Using RSM, researchers can develop predictive models that accurately estimate curcumin yield under different extraction conditions.

7.2.2 Artificial neural networks (ANN)

According to Basheer and Hajmeer (2000), Artificial Neural Networks are another effective optimisation approach utilised in current extraction research. The architecture and operation of the human brain serve as inspiration for ANN, a computer modelling approach. When trying to model multivariate, complex, nonlinear interactions, it really shines. Experimental data like extraction duration, solvent concentration, temperature, and particle size are used to train ANN models for extraction operations. Next, the trained network will forecast the curcumin yield based on various parameter combinations.

Compared with traditional statistical models, ANN offers several advantages:

- Ability to handle nonlinear relationships
- Higher prediction accuracy
- Capability to model complex interactions between variables

As a result, ANN has increasingly been used in combination with RSM to optimize extraction processes for phytochemicals (Basheer and Hajmeer, 2000).

7.3 Importance of process optimization

Industrial curcumin production relies heavily on process optimisation, which cuts down on operational costs and environmental impact while increasing extraction efficiency (Chemat *et al*., 2017). Increased yields, decreased solvent consumption, and decreased processing times can be achieved by optimising extraction parameters in industrial settings. In addition, Azmir *et al*. (2013) found that pharmacological, nutraceutical, functional food, and cosmetic applications could benefit from curcumin extracts made using optimised extraction procedures. The combination of powerful statistical and computational optimization tools consequently represents a key step toward the development of efficient and sustainable curcumin extraction systems.

8. Industrial applications of curcumin

Gupta *et al*. (2013) and Hewlings and Kalman (2017) note that curcumin, the main bioactive molecule extracted from *C. longa* rhizomes, has a wide range of biological activity and functional qualities, making it an important industrial ingredient. The spice curcumin has expanded its uses beyond its traditional culinary and medicinal applications to encompass the pharmaceutical, nutraceutical, food processing, and cosmetics sectors (Prasad *et al*., 2014). Anand *et al*. (2007) and Gupta *et al*. (2013) note that this natural molecule is highly sought after for its medicinal, antibacterial, anti-inflammatory, and antioxidant capabilities, which have led to the development of novel health and wellness products. The increasing demand for curcumin in the industrial sector has been driven by the rising demand for natural, plant-based products among consumers (Hewlings and Kalman, 2017). Chemat *et al*. (2017) noted that recent developments in extraction methods and formulation strategies have made it possible to produce curcumin of an industrially acceptable purity on a wide scale. Table 2 summarises the various industrial uses of curcumin in the pharmaceutical, nutraceutical, food, and cosmetic industries.

Table 2: Industrial applications of curcumin across different sectors

Industry	Application area	Function of curcumin	Example products
Pharmaceutical industry	Drug deve1opment and therapeutic formulations	Anti-inflammatory, Antioxidant, Anticancer, Antimicrobial, Neuroprotect iveproperties	Capsules, tablets, nanoparticles, liposomal drugformulations, anti-inflanmatory medications
Nutraceutical industry	Dietary supplements and functional health products	Supports immunefunction, reduces inflammation, improves metabolic health	Curcumin capsules, curcum in-piperine supplements, herbal health drinks, nutraceutical powders
Food industry	Natural food colorant and functional food additive	Provides yellow color, antioxidant activity, improves shelf-life	Dairy products, beverages, sauces, confectionery products, functional foods
Cosmetic industry	Skincare and personal care formulations	Antiageing, Anti-inflammatory, Antimicrobial, Skin protection	Face creams, lotions, serums, herbal facemasks, antiacne skin care products

9. Regulatory aspects, safety, and approval guidelines for curcumin

Curcumin has gained global regulatory acceptance as a natural food additive, nutraceutical ingredient, and therapeutic compound. However, its application across industries is governed by different regulatory frameworks depending on the intended use.

9.1 Global regulatory status

The usage of curcumin as a natural food dye and ingredient has received widespread approval. This product has been given the GRAS (Generally Recognised As Safe) label by the FDA in the US. The European Food Safety Authority (EFSA) has given curcumin their stamp of approval as a food additive in the European Union, specifically under code E100. There are certain limits to how much curcumin can be used in food products in India, but the FSSAI has given the go-ahead. Table 3 displays the use limitations and acceptable daily intake (ADI).

9.2 Safety and toxicological considerations

Curcumin has few negative effects and low toxicity when taken as directed. However, at higher concentrations, it may exhibit:

- Gastrointestinal disturbances
- Poor bioavailability
- Rapid metabolism and systemic elimination

Dosage optimisation and formulation strategies are crucial in product development, as these considerations emphasise.

Table 3: Acceptable daily intake (ADI) and usage limits

Regulatory body	Acceptable daily intake (ADI)	Application
JECFA (FAO/WHO)	0-3 mg/kg body weight	Food additive
EFSA	0-3 mg/kg body weight	Food colorant (E100)
FSSAI	As per GMP guidelines	Food and nutraceuticals

9.3 Regulatory challenges in curcumin applications

Despite its approval, several challenges limit its broader regulatory acceptance, particularly in pharmaceuticals:

- Variability in purity and composition of extracts
- Residual solvent toxicity in conventional extraction methods
- Poor aqueous solubility and low bioavailability
- Lack of standardized extraction and processing protocols

9.4 Relevance of extraction technologies to regulatory compliance

In order to achieve regulatory criteria, the extraction procedure chosen is critical. There are several benefits to using modern, environmentally friendly extraction methods:

- **Reduced solvent residues**, ensuring compliance with safety regulations
- **Higher purity and consistency**, facilitating standardization
- **Environmentally sustainable processing**, aligning with global regulatory trends

The utilisation of green solvents (ionic liquids and deep eutectic solvents), ultrasound-assisted extraction, and supercritical fluid extraction are some of the emerging approaches that are gaining popularity for their capacity to create high-quality curcumin that is acceptable for usage in food and pharmaceutical applications.

10. Challenges and future perspectives

Gupta *et al*. (2013) and Hewlings and Kalman (2017) note that curcumin's extraction, purification, and industrial use have come a long way, but that the spice has not yet reached its full commercial potential due to a number of scientific and technological obstacles. Physicochemical and technological constraints frequently limit the practical application of curcumin, the principal bioactive component isolated from *C. longa* rhizomes, despite its impressive functional and pharmacological characteristics (Anand *et al*., 2007). In order to optimise curcumin production, increase its biological efficacy, and pave the way for large-scale industrial uses, it is crucial to tackle these issues. Accordingly, new studies have concentrated on finding creative ways to circumvent these restrictions and increase curcumin's application across a range of industries (Prasad *et al*., 2014).

10.1 Low bioavailability of curcumin

The low bioavailability of curcumin in humans is a major problem (Anand *et al*., 2007; Hewlings and Kalman, 2017). The term ''bioavailability'' describes how much of a chemical is able to enter the bloodstream and exert its biological effects. There are a number of reasons why curcumin has a low bioavailability, such as its fast metabolism, rapid systemic excretion, and poor water solubility. The content of curcumin in the bloodstream is drastically reduced after oral consumption because it is transformed metabolically in the intestines and liver (Anand *et al*., 2007). The hydrophobic properties of curcumin also make it difficult for it to dissolve in water, which means less of it may be absorbed by the body through the digestive system. According to Moghadamtousi *et al*. (2014), researchers have investigated a range of formulation options to address this constraint, including nanoemulsions, liposomes, micelles, and polymer-based delivery systems. These methods are designed to improve the pharmacological and nutraceutical efficacy of curcumin by making it more soluble, stabilising it, and increasing its absorption.

10.2 Stability issues

Priyadarsini (2014) notes that curcumin's chemical instability under specific environmental conditions is another significant hurdle. A number of environmental conditions, including light, oxygen, an acidic pH, and high temperatures, can affect curcumin's activity. Degradation or structural alteration of the chemical, leading to diminished biological activity, can occur under these conditions. As an example, curcumin has the potential to degrade through hydrolysis or oxidative processes in food processing or in conditions with a high pH (Wang *et al.*, 1997). Degradation of curcumin-containing products lowers the concentration of active chemicals and may alter their colour and functional characteristics as well. Encapsulation, microencapsulation, and coating systems based on polymers are among the protective technologies that researchers are looking at to increase stability (Moghadamtousi *et al.*, 2014). In culinary, pharmaceutical, and cosmetic applications, these methods help preserve curcumin from environmental degradation and extend its shelf life.

10.3 High cost of advanced extraction technologies

High operational and capital costs frequently prevent advanced extraction methods like ultrasonic-assisted, microwave-assisted, and supercritical fluid extraction from being widely used in industry, despite the fact that they offer better efficiency and higher curcumin yields (Chemat *et al.*, 2017). These technologies can be more expensive than traditional extraction methods due to the specialised equipment installation, energy needs, and maintenance costs. These expenses might make it difficult, if not impossible, for small and medium-sized businesses to invest in modern extraction methods. Accordingly, improving process efficiency, decreasing energy consumption, and creating extraction systems that are cost-effective enough for commercial-scale operations should be the focus of future research (Azmir *et al.*, 2013).

10.4 Difficulties in industrial scale implementation

A further significant obstacle is the transition from experimental extraction to industrial-scale manufacturing (Azmir *et al.*, 2013). When employed on a big industrial scale, many extraction procedures that work well in small-scale investigations might become inefficient. When planning to scale up an extraction system, it is important to think about things like solvent recovery, energy efficiency, process control, and equipment design. Also, producers still very care about making sure that their products stay pure and of high quality even when processing them on a massive scale. As a result, improving curcumin industrial production efficiency requires the creation of scalable extraction methods and integrated processing systems.

11. Future perspectives

Despite the challenges discussed above, ongoing research and technological innovations are expected to significantly improve the production and utilization of curcumin in the future (Prasad *et al.*, 2014). Several emerging approaches show promising potential for addressing the current limitations associated with curcumin extraction and application.

11.1 Hybrid extraction technologies

To improve extraction efficiency and save processing time, hybrid extraction technologies combine two or more extraction processes (Chemat *et al.*, 2017). A few examples of methods that can greatly enhance the release of curcuminoids from plant matrices include merging ultrasound with microwave-assisted extraction or combining enzyme-assisted extraction with supercritical fluid extraction. Improved mass transfer, more efficient disruption of plant cell structures, and higher extraction yields can all be achieved through the use of these hybrid techniques. These technologies have the potential to provide realistic answers for enhancing curcumin production on a large scale.

11.2 Nanoencapsulation strategies

According to Moghadamtousi *et al.* (2014), nanoencapsulation is a highly promising method for increasing the stability and bioavailability of curcumin. Here, polymeric nanoparticles, solid lipid nanoparticles, nanoemulsions, or curcumin molecules are enclosed within nanoscale carriers. The benefits of nanoencapsulation include better absorption in biological systems, controlled release, protection from environmental deterioration, and greater solubility. Pharmaceutical, nutraceutical, and functional food applications are where nanoencapsulation really shines due to these characteristics.

11.3 Sustainable green solvents

Future research should also focus on developing extraction solvents that are less harmful to the environment (Chemat *et al.*, 2017). Sustainable phytochemical extraction has shown great promise for green solvents including natural deep eutectic solvents and deep eutectic solvents. The low toxicity, biodegradability, and enhanced extraction efficiency are just a few of the benefits offered by these solvents. One way to make curcumin extraction more environmentally friendly is to use green solvents in conjunction with other cutting-edge extraction techniques.

11.4 AI based process optimization

The optimisation of extraction procedures is anticipated to be greatly impacted by the application of artificial intelligence and machine learning approaches (Basheer and Hajmeer, 2000). Machine learning algorithms, data-driven optimisation, predictive modelling, and other computational methods can find the best extraction conditions far faster than old-fashioned experiments. In order to forecast how various process factors will affect extraction efficiency, artificial intelligence can sift through massive datasets produced by experimental investigations. In addition to boosting the accuracy of process optimisation, these methods have the potential to drastically cut down on experimental time and expense.

The fields of engineering, pharmaceuticals, and food science all work together closely in curcumin research. Yield, purity, and stability of curcumin are determined by extraction processes that have been created using engineering approaches. The bioavailability, therapeutic efficacy, functioning, and stability of this compound in food systems are all affected by these parameters. Hence, for both process efficiency and curcumin's general applicability across many industries, it is crucial to select and optimise extraction methods.

12. Conclusion

The outstanding medicinal capabilities and diverse industrial applications of curcumin have propelled it to the status of a very valued phytochemical. An essential component in the pharmaceutical, nutraceutical, culinary, and cosmetic sectors, this bioactive chemical is derived from the rhizomes of *C. longa* and has shown remarkable antioxidant, anti-inflammatory, antibacterial, and anticancer actions. Soxhlet and solvent extraction are two of the most used traditional methods for curcumin recovery. However, these procedures have a number of drawbacks, such as high solvent consumption, lower efficiency, and lengthy extraction times.

New extraction methods include pressurised liquid extraction, enzyme-assisted extraction, supercritical fluid extraction, ultrasound-assisted extraction, and microwave-assisted extraction have emerged thanks to developments in food and process engineering. These methods are more sustainable, take less time to process, and improve extraction efficiency. The use of deep eutectic solvents and other green solvents has also helped advance extraction methods that are gentler on the environment.

The high expense of sophisticated extraction methods, curcumin's poor bioavailability, and stability constraints are some of the remaining obstacles, notwithstanding these improvements. Further investigation into innovative delivery systems, enhanced extraction methodologies, and scalable industrial processes is necessary to tackle these difficulties. The existing constraints of curcumin utilisation can be overcome with the help of emerging methodologies including hybrid extraction technologies, nanoencapsulation systems, and process optimisation based on artificial intelligence. Finally, establishing sustainable, efficient, and scalable methods for extracting and applying curcumin will require ongoing multidisciplinary research combining phytochemistry, food engineering, and biotechnology. These developments bode well for the future of curcumin, as they should increase its commercial and medicinal applications.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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