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Extraction, purification and applications of curcumin from plant materials-A
comprehensive review

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1 **Abstract**

2 *Background:* Curcumin is a safe substance that is used as food cosmetic additive and
3 pharmaceutical product. Obtaining pure curcumin from plant sources is very important for
4 fundamental research as well as for the above applications. Efficient extraction and purification
5 methods, which meet green chemistry criteria including safety, environment-friendliness,
6 economic requirements, and process efficiency are needed.

7 *Scope and approach:* This review provides an up-to-date and comprehensive summary of the
8 various methods used for extraction and purification of curcumin from plant materials, and its
9 various applications in food, cosmetics and pharmaceutical fields.

10 *Key findings and conclusions:* Many different extraction methods ranging from conventional
11 techniques (e.g. soxhlet extraction, maceration and solvent extraction) to advanced extraction
12 technologies (e.g. ultrasound-assisted extraction, microwave-assisted extraction, enzyme-
13 assisted extraction, supercritical liquid extraction, etc.) have been exploited to obtain curcumin
14 from plant materials. Various other substances co-exist with curcumin in crude extracts. Many
15 different purification techniques, alone or in combination, have been investigated for isolation
16 and purification of curcumin from curcumin extracts or commercially available crude curcumin.
17 These include conventional techniques (e.g. column chromatography, semi-preparative high
18 performance liquid chromatography) and supplementary modern techniques (e.g. high-speed
19 counter-current chromatography, supercritical fluid chromatography). To recover curcumin
20 from plant materials, selection of apposite routes based on novel technologies (both in
21 extraction and purification) is important to maximize efficiency, to decrease use of toxic solvent,
22 as well as to reduce the processing time and energy consumption. Additionally, various potential
23 or commercial uses of curcumin are reviewed.

24 **Keywords:** Curcumin; Extraction; Purification; Applications

25

26 **1. Introduction**

27 Curcumin, also known as diferuloylmethane, is a hydrophobic polyphenol derived from the
28 rhizome of perennial herbs genus *Curcuma* which belongs to the ginger family (Zingiberaceae)
29 and includes species like *Curcuma longa*, *Curcuma amada*, *Curcuma zedoaria*, *Curcuma*
30 *aromatic*, *Curcuma raktakanta*. Among these species, *Curcuma longa* (turmeric) is the most
31 popular. Generally, turmeric rhizomes contain 3-5% of three types of curcuminoid derivatives
32 including curcumin (75%), demethoxycurcumin (10-20%) and bisdemethoxycurcumin (5%),
33 curcumin being the most important bioactive compound (Shirsath et al., 2017; Wakte et al.,
34 2011).

35 Curcumin has long been used as a spice and a natural coloring agent in Indian curries, as well
36 as a component of Chinese traditional medicines. As a food additive, its E number (codes for
37 substances used as food additives for use within the European Union (EU) and European Free
38 Trade Association (EFTA)) is E100. In recent years, numerous *in vivo* and *in vitro* studies have
39 revealed that curcumin has various physiologic activities, and worldwide attention has therefore
40 been focused on curcumin. Curcumin has been found to have multiple actions such as anti-
41 oxidant through scavenging of free radicals (Meghana et al., 2007), anti-inflammatory by
42 suppression of NF-kB and AP-1 activation (Kang et al., 2004), anti-cancer through inhibition
43 of cancer cell proliferation, induction of apoptosis, suppression of angiogenesis, inhibition of
44 the expression of anti-apoptotic proteins, protection of the immune system (Dorai et al., 2001;
45 Sa & Das, 2008), and anti-bacterial/fungal/viral activities (Liu & Huang, 2013; Rafiee et al.,
46 2019). Due to its wide range of pharmacological activities, curcumin shows potential for
47 commercial use in different industries including food, cosmetics and pharmaceuticals.

48 There are two methods for obtaining curcumin: by means of synthesis and by extraction from
49 plants. Many authors have described the preparation of synthetic curcumin (Pabon, 2010;
50 Rodrigues et al., 2015). Nevertheless, obtaining curcumin, which is naturally present in plants

51 by means of extraction still represents the most economical way for curcumin production. To
52 date, various extraction techniques ranging from conventional (e.g. soxhlet extraction,
53 maceration and solvent extraction) (Paulucci et al., 2013; Shirsath et al., 2017; Silva et al., 2005)
54 to advanced extraction technologies (e.g. ultrasound-assisted extraction, microwave-
55 assisted extraction, enzyme-assisted extraction, supercritical liquid extraction, etc.) (Gökdemir
56 et al., 2020; Kwon & Chung, 2015; Sahne et al., 2016; Shirsath et al., 2017; Wakte et al., 2011)
57 have been reported for efficient extraction of curcumin from plant materials. It is stated that the
58 extraction procedure plays a critical role in determining the quantity and quality of bioactive
59 compounds. In order to obtain high yield and high quality curcumin, it is very important to
60 choose appropriate and effective methods and operate these under optimal conditions.

61 In general, various substances including essential oil, sugar, its derivatives demethoxycurcumin
62 (DMC) and bisdemethoxycurcumin (BDMC), and other small molecules co-exist in crude
63 curcumin extracts. Commercially available crude curcumin usually contains variable amounts
64 of other two compounds, typically about 16-26 % DMC and 2-8% BDMC (Horosanskaia et al.,
65 2020). Consequently, many different purification techniques, alone or in combination, have
66 been exploited to isolate and purify curcumin from curcumin extracts or commercially available
67 crude curcumin. Conventional purification techniques (e.g. column chromatography, semi-
68 preparative high performance liquid chromatography) as well as supplementary modern
69 techniques (e.g. high-speed counter-current chromatography, supercritical fluid
70 chromatography, etc.) have been used to separate and purify curcumin.

71 Obtaining curcumin from plant sources is very important for fundamental research, and for
72 practical applications in food, cosmetics and pharmaceutical fields. However, its application
73 has remained challenging due to some of its properties, i.e., poor water solubility, chemical
74 instability, photo degradation, relatively high rate of metabolic degradation, and low
75 bioavailability. Therefore, numerous studies have attempted to address these specific challenges

76 using methods such as encapsulation. The strategies used to overcome the physicochemical
77 challenges with curcumin were recently comprehensively covered in several research reviews
78 (Araiza-Calahorra et al., 2018; Jiang et al., 2020; Rafiee et al., 2019) and therefore will not be
79 discussed in this paper. This review instead focuses on the extraction and purification
80 methodologies used for purification of curcumin for its application in food, cosmetics and
81 pharmaceutical industries.

82 **2. Curcumin extraction techniques**

83 Extraction is the first and foremost step in the recovery of curcumin from plants materials. All
84 extraction methods were developed based on some common objectives, such as (a) to recover
85 targeted compounds from plants materials, (b) to increase the selectivity of the extraction
86 procedure, (c) to improve the extraction efficiency, and (d) to provide a stable and reproducible
87 approach (Zhang et al., 2019).

88 Conventional extraction methods, such as Soxhlet extraction, maceration or solvent extraction,
89 are widely used to extract curcumin from plants. These methods are simple, but are generally
90 non-selective, are time consuming and in some cases cause degradation of heat-sensitive
91 substances (Zhang et al., 2019). To surmount such obstacles, novel extraction methods such as,
92 ultrasound-assisted extraction, microwave-assisted extraction, enzyme-assisted extraction, and
93 supercritical liquid extraction have been developed as more efficient alternatives to
94 conventional extraction. These advanced techniques, which are regarded as eco-friendly green
95 technologies exhibit potential for extraction of curcumin from plant materials. Some recent
96 examples of techniques used for the extraction of curcumin are described in following sections
97 (summarized in **Table 1**). Moreover, schematic diagrams of experimental set-ups used for
98 conventional extraction (**Fig. 1a**) and advanced extraction (**Fig. 1b**) are presented.

99 **2.1. Conventional methods for extraction of curcumin**

100 Solvent extraction of solid samples, which is commonly known as “solid-liquid extraction”,

101 (also referred to as “maceration” or “soaking”), is a well-understood and widely-used method.
102 An extensive range of solvents including non-polar organic solvents and a combination of
103 organic solvents and water has been used to extract curcumin from plants (Paulucci et al., 2013;
104 Popuri & Pagala, 2013). Popuri & Pagala (2013) carried out a comparison of extraction solvents
105 (acetone, ethyl acetone, ethanol, methanol, and isopropanol) for isolation of curcumin from
106 *Curcuma Longa* L. It was found that extraction with ethanol gave the highest yield (0.26 mg/10
107 g) when the extraction was performed at 30°C for 1 h with a solid to solvent ratio of 1:8.
108 Consistent with this, ethanol was the most preferred solvent for extraction of curcumin among
109 all organic solvents employed (Paulucci et al., 2013; Shirsath et al., 2017; Sogi et al., 2010).
110 Moreover, the ethanol concentration of the solvent mixture plays a crucial role in determining
111 the extraction efficiency (Paulucci et al., 2013).

112 Soxhlet extraction, which is regarded as the standard and reference method for solid-liquid
113 extraction of bioactive compounds from plants was developed by German chemist Soxhlet in
114 1879. Extraction of curcumin from plants using Soxhlet extractor has been reported by several
115 authors (Dutta, 2015; Shirsath et al., 2017). For instance, Shirsath et al. (2017) compared
116 extraction yield of curcumin resulting from Soxhlet extraction, maceration extraction and UAE
117 and found that Soxhlet extraction produced a higher curcumin extraction rate than UAE and
118 maceration extraction. However, Soxhlet extraction was carried out at much higher temperature
119 and for very long duration as compared to UAE. In order to improve the performance of Soxhlet
120 extraction, high-pressure Soxhlet extraction, automated Soxhlet extraction, ultrasound-assisted
121 Soxhlet extraction and microwave-assisted Soxhlet extraction have been developed (see (Luque
122 de Castro & Priego-Capote, 2010) and references therein), which have decreased or minimized
123 the negative aspects of the conventional Soxhlet extractor.

124 Hydro/steam distillation is another traditional extraction method in use for extraction of
125 bioactive compounds and essential oils. It has been applied to remove essential oil (turmeric

126 flavor) from crude turmeric powder or turmeric oleoresin, so as to obtain flavor-free, turmeric
127 or curcumin. In a study conducted by Silva et al. (2005), good yield of the deodorized turmeric
128 was obtained after hydro-distillation and the cost was much lower than purified curcuminoid
129 pigments. Moreover, deodorized turmeric had similar curcuminoids levels compared to the
130 control and to a sample deodorized by hexane extraction. These results indicated that the hydro-
131 distillation method is an efficient method to obtain turmeric powder or curcuminoids with less
132 residual turmeric flavor, without any pigment loss.

133 2.2. Novel methods for extraction of curcumin

134 2.2.1. Ultrasound-assisted extraction (UAE)

135 Ultrasound works on the principle of tandem compression and expansion induced by sound
136 waves with the frequency range of 20 kHz-100 MHz. The ultrasonic waves induce micro
137 bubbles formation, and the breakage of these bubble lead to cavitation phenomenon, which
138 results in intense shear forces, shock waves, macro-turbulences, micromixing and acoustic
139 streaming (Zhang et al., 2019). In the process of sonication, motion energy transforms into heat,
140 which acts as activation energy for initiating some physicochemical reactions which promote
141 mass transfer (Garavand et al., 2019). Based on this theory, UAE has been developed to release
142 favorable and desired compounds from plant materials by accelerating diffusion, increasing
143 mass transfer and speeding up the contact of the solvent to the target compounds.

144 In UAE, the operational variables including the applied frequency, temperature and time, the
145 properties of extraction solvent, and the features of plant material are important factors that
146 affect the yield of curcumin. Thus, it is advisable to optimize the UAE process before it is
147 applied to recover curcumin. Shirsath et al. (2017) investigated the effect of operating
148 parameters on the curcumin extraction yield using UAE and found that the optimum parameters
149 for such extraction were 35 °C, solid/solvent ratio of 1:25 (g/mL), particle size of 0.09 mm, 1 h
150 extraction time, ultrasonic power of 250 W and ultrasound frequency of 22 kHz with ethanol

151 as the solvent. The obtained yield (72%) was significantly higher than solvent extraction or
152 maceration/soaking where only about 62% yield was achieved in an 8 h process. This results
153 indicated that it can be a rapid and sustainable alternative process compared with conventional
154 procedures.

155 Additionally, environmentally friendly and energy saving pulsed UAE has been used for
156 curcumin extraction, and promising results suggested pulsed UAE is a good choice to obtain
157 curcumin with high extraction rate but low energy consumption. In pulsed UAE, the duration
158 and interval time had a remarkable influence on the extraction. It was found the yield of
159 curcuminoids tended to decrease with the increase of interval time (M. Li et al., 2014).
160 Therefore, high yield of curcumin can be produced by reducing the pulsed duration or interval
161 time. Under optimum conditions, Li et al. (2014) found that the curcumin yield obtained in the
162 pulsed UAE (1.03 ± 0.02 g/100 g dry weight) was more efficient than that in UAE (0.82 ± 0.01
163 g/100 g dry weight).

164 2.2.2. Microwave-assisted extraction (MAE)

165 MAE is a well-established, automated, green extraction method for bioactive compounds
166 extraction which uses microwave energy (electromagnetic waves with a frequency range of 300
167 MHz to 300 GHz). Generally, microwave frequency associated with lab work and domestic
168 work is 2.45 GHz (Garavand et al., 2019). The dispersal of electromagnetic waves induces
169 microwave heating which results in an accelerated mass and heat transfer, leading to better
170 transport of solutes from the inside of plant materials to the extracting solvent medium (Praveen
171 et al., 2019). Notably, MAE offers some advantages, including the combined reduction of the
172 extraction time, solvent and energy consumptions, and produces a higher yield as compared to
173 conventional methods (Mena-García et al., 2019).

174 In recent years, MAE method has been applied to recover curcumin from plant materials at
175 various operating conditions. The microwave power, time intervals (irradiation time and

176 cooling time), temperature, size of plant materials and type of solvent are the main variables
177 investigated by researchers for the extraction of curcumin. In some cases, dry microwave
178 irradiation (which enhances the degradation of cell wall) and pretreatment of the powdered
179 sample (which makes the sample more vulnerable to microwave heating) are added to the MAE
180 process, which can increase both extraction rate and extraction efficiency (Mandal et al., 2008;
181 Wakte et al., 2011). For example, Mandal et al. (2008) performed a Taguchi L9 orthogonal
182 design using microwaves based on solvent–sample duo-heating synergism, for the extraction
183 of curcumin from *Curcuma longa* L. The optimum conditions were as follows: 140 W (20%)
184 microwave power, 4 min irradiation time, particles screened through sieve 20, 8 mL of modifier
185 (methanol) and solid to solvent (acetone) ratio of 1:20. This resulted in 4.98% curcumin yield,
186 which was higher than that with Soxhlet extraction, maceration and stirring extraction.

187 The above examples revealed that extraction of curcumin by MAE had better precision and
188 higher yield with significant reduction in extraction time, when compared to conventional
189 approaches. Additionally, the MAE technique was more efficient (in terms of percent yield and
190 required extraction time) when compared to ultra-sonic and supercritical carbon dioxide
191 assisted extraction (Wakte et al., 2011; Li et al., 2014).

192 2.2.3. Enzyme-assisted extraction (EAE)

193 Plant cell walls consist of a series of complex structural polysaccharides, conferring cells
194 stability and resistance to the extraction of the intracellular components. Thus, enzymes with
195 specific hydrolytic properties are used to break down the matrix of the plant cell wall in order
196 to gain access to the bioactive components within the cytosolic spaces and even those bound to
197 the cellular walls. In EAE method, enzymes such as α -amylase, glucoamylase, and
198 amyloglucosidase are used for the extraction of curcumin (Kurmudle et al., 2011; Kurmudle et
199 al., 2013; Sahne et al., 2016, 2017). This approach is gaining more attention because it is
200 efficient, simple, sustainable and eco-friendly.

201 It is important to note that enzyme specificity and selectivity are influenced by multiple factors
202 such as temperature, time, pH and enzyme concentration. Therefore, the use of optimum
203 enzyme reaction conditions is necessary for getting the maximum hydrolytic activity. Kurmudle
204 et al. (2013) performed a single factor approach to evaluate effect of different enzyme reaction
205 conditions on the recovery of curcuminoids and found 3% α -amylase used at pH 5.0 with 5 h
206 of incubation, 8 h of extraction and 2% glucoamylase used at pH 4.5 with 5 h of incubation, 8 h
207 of extraction, with acetone as a solvent, increased the yields of curcumin by 26.04% and 31.83%
208 when compared to their control. Sahne et al. (2016) also optimized the process parameters in
209 order to obtain maximum yield of curcumin and found that the application of α -amylase and
210 amyloglucosidase on turmeric powder gave 4.1% curcumin extraction yield using EAE under
211 optimum conditions.

212 In some cases, EAE is combined with other extraction techniques such as ionic liquid extraction
213 and three phase partitioning. Sahne et al. (2017) used enzyme-assisted ionic liquid extraction
214 to extract curcumin from turmeric. In their work, carbamate ionic liquid extraction of curcumin
215 from enzyme pretreated turmeric (α -amylase and amyloglucosidase mixture: substrate =1:25,
216 incubation at 65°C for 6 h) resulted in a curcumin yield of 5.73% at 25 °C, the extraction time
217 being 2 h.

218 2.2.4. Pressurized liquid extraction (PLE)

219 PLE is an attractive green-technology that uses liquid solvents at temperatures above their
220 atmospheric boiling point, i.e. at high temperature-pressure conditions below their critical point
221 for the extraction of bioactive compounds (Osorio-Tobón et al., 2016). Elevated temperature
222 and high pressure applied in the PLE process increase solubility and mass transfer rates between
223 the plant matrix and the solvent, which improve the extraction performance (Ameer et al., 2017).
224 If water is used as the extraction solvent, this green technique is also referred as subcritical
225 water extraction (SWE) or pressurized hot water extraction. Subcritical water is an effective

226 extraction solvent for extracting various medium and low polarity compounds because the
227 decreased dielectric constant of subcritical water is similar to that of organic solvents.

228 In the past few years, some applications of SWE for curcumin extraction have been reported in
229 the literature, which indicated that SWE can be a rapid and sustainable alternative process
230 compared with conventional procedures. A selection of recent applications of SWE is listed in
231 **Table 1**. These studies involved the optimization of the extraction conditions (e.g., temperature,
232 pressure, extraction time and flow rate). This is important because the polarity of water
233 modulated by the extraction process parameters, then influence extraction efficiency. In a study
234 conducted by Kiamahalleh et al. (2016), the influences of SWE conditions (e.g. particle size:
235 0.6-2 mm, extraction temperature: 120-160 °C, pressure:10-25 bar and retention time: 6-22 min)
236 on curcumin yield from deflavored turmeric were investigated. The authors obtained 3.8 wt%
237 of curcumin from *Curcuma longa* L. under optimized conditions (particle size of 0.71 mm,
238 temperature of 140 °C, pressure of 10 bar, and extraction time of 14 min). Moreover, they
239 demonstrated that the changes in porosity and hardness of turmeric was directly related to the
240 amount of extracted curcumin.

241 The addition of co-solvents or additives such as salts or buffers in SWE has been found to
242 improve extraction yields. Euterpio et al. (2011) evaluated the feasibility of using subcritical
243 water to extract curcumin from turmeric by adjusting its pH at extreme values. Also, the effect
244 of temperature, and buffer concentration on the curcumin extraction yield were investigated in
245 detail. It was found that the optimum conditions for such extraction were at a temperature of
246 197 °C using 62 g/L phosphate-buffered water at pH 1.6. Their results demonstrated that the
247 extraction yields were improved when the pH was adjusted to a very low value. In another study
248 (Kwon & Chung, 2015), subcritical water was used in combination with ethanol for extracting
249 curcumin from turmeric; and the authors found that the concentration of extracted curcuminoids
250 gradually increased with the ethanol content. Moreover, this technique was also tested for scale-

251 up. It was found that pilot-scale extraction (8 L scale) (13.58% in dried extracts) gave recoveries
252 comparable to those obtained in lab-scale extraction (0.1 L scale) (15.80% in dried extracts)
253 under the optimal conditions (extraction temperature of 135 °C, extraction time of 5 min,
254 mixture ratio of 1:20 (w/v) for solid and solvent, and the use of 50% ethanol as solvent).

255 2.2.5. Supercritical fluid extraction (SFE)

256 SFE is the most common non-conventional technique used industrially on a large scale which
257 utilizes supercritical fluids as extraction solvents. Supercritical carbon dioxide (CO₂) is one of
258 the most commonly used extraction solvents, which is known as a green solvent without any
259 toxicity and side effects (Garavand et al., 2019; Li et al., 2019). The efficiency of supercritical
260 CO₂ comes from its physical and thermal properties, which incorporates the features of both
261 liquid and gaseous states (Belwal et al., 2020). A supercritical fluid can be obtained when the
262 temperature and pressure of a gas or a liquid exceed its critical points (Guiochon & Tarafder,
263 2011). In SFE process, the mild processing temperature required make it suitable for extraction
264 of thermally unstable and easily oxidized compounds. Generally, SFE is regarded as a green
265 alternative method to conventional extraction as it reduces amount of solvent required, shortens
266 extraction time, facilitates automation, and improves selectivity (Garavand et al., 2019).

267 Supercritical CO₂ is endowed with a high solvating capacity for essential oils (low polarity
268 molecules), while it has limited capacity for curcumin (being more polar). Therefore, SFE using
269 CO₂ is a suitable method for extraction of essential oil from *Curcuma longa* L., but the amounts
270 of curcumin which is extracted using pure CO₂ is low. Therefore, polar organic co-solvents (or
271 modifiers), such as methanol, ethanol, are added in small quantities to improve the extraction
272 efficiency of curcumin. For instance, Wakte et al. (2011) developed a methodology to extract
273 curcumin from *Curcuma longa* L. using supercritical CO₂ with 10% ethanol and obtained 1.46 %
274 curcumin yield at a pressure of 30 MPa, temperature of 50 °C, CO₂ flow rate of 5 mL/min and
275 extraction time of 300 min.

276 Alternatively, other methodologies based on the combination of SFE following PLE have been
277 proposed for the extraction of curcumin from plant materials. The essential oil was removed
278 initially from the turmeric rhizomes powder by extraction with supercritical CO₂ (Osorio-Tobón
279 et al., 2014, 2016). Immediately after the SFE process, PLE can be performed using ethanol as
280 the solvent to extract curcumin. In the study conducted by Osorio-Tobón et al. (2014), PLE was
281 applied to recover curcumin after the SFE process was completed. Similar curcumin yields
282 (4.3%) were obtained by this process, Soxhlet extraction and low-pressure solvent extraction,
283 but turmeric essential oil can be recovered in the SFE process. Later, Osorio-Tobón et al. (2016)
284 investigated SFE, PLE and supercritical antisolvent process in order to obtain turmeric essential
285 oil and powdered curcuminoid-rich extract, and found the integration processes enabled to
286 obtain high extraction yield of both curcumin (7.6%) and essential oil (6.4%) in a more
287 economical way. Therefore, production of curcumin through integrated process is economically
288 viable and shown to be promising.

289 2.2.6. Ionic liquids-based extraction

290 In recent years, “green solvents” have been preferred instead of the classical organic solvents
291 in order to prevent environmental pollution. In this regards, ionic liquids have gained
292 considerable attention due to their unique chemical and physical properties such as negligible
293 volatility, good thermal stability, tunable viscosity, and preservation of biological activities
294 (Pandey, 2006; Passos et al., 2014). Based on their properties, ionic liquids have been
295 successfully applied in various applications such as synthesis, catalysis, analysis and separation
296 processes.

297 Combination of ionic liquids with other extraction methods, such as UAE, MAE and EAE, have
298 been used for curcumin extraction, and promising results indicated that ionic liquids based
299 extraction methods not only can reduce environmental impact, but also can improve extraction
300 efficiency. Xu et al. (2015) investigated hydrophilic ionic liquids [Bmim]Br, [Him]Br,

301 [Omim]Br, and [Omin][BF₄] as the solvents for the UAE of curcuminoids from turmeric and
302 found the curcuminoids yield was 6.14%, which was higher than that with 85% ethanol-based
303 UAE (4.40%) and 85% ethanol-based heat-reflux extraction (5.12%). In the study of Sahne et
304 al. (2017), carbamate ionic liquid-based EAE was used for extraction of curcumin from α -
305 amylase and amyloglucosidase enzymes pretreated turmeric resulting in extraction yield of
306 5.73%, while the extraction rate was only 3.11% when acetone was used for extraction of
307 curcumin from pretreated turmeric at the same operation conditions (25 °C and 2 h). In another
308 study (Liang et al., 2017), ionic liquid [OMIM][Br]-based MAE was successfully applied for
309 extracting curcuminoids from *Curcuma longa* L.. It was found that the effect of [OMIM][Br]
310 on the MAE of curcuminoids was similar to that of ethanol (75% and 100%) and methanol (75%
311 and 100%) when all extractions were applied under optimum conditions. ionic liquid based
312 extraction is a step towards development of an energy-saving extraction process, with rapid
313 dissolution of curcumin and least harmful effects on the environment.

314 **3. Curcumin purification techniques**

315 After successful extraction by different methods, curcumin is subjected to further separation
316 and purification. Based on factors such as polarity, ligand interaction, and solubility, a series of
317 purifying methods, including column chromatography, semi-preparative high performance
318 liquid chromatography, high-speed counter-current chromatography, preparative supercritical
319 fluid chromatography and crystallization, have been developed for isolation and purification.
320 The methods used to separate and purify curcumin from extracts or commercial crude curcumin
321 are described in the following sections (summarized in **Table 2**). A schematic diagram of the
322 experimental set-up for purification methods is also presented (**Fig. 2**).

323 **3.1. Column chromatography (CC)**

324 Column chromatography is the most common method for purification of substances at a
325 preparative scale. The procedure involves preparation of the column, loading the sample onto

326 the column, eluting the column by the mobile phase and recovering the constituents (Cvetković
327 et al., 2020). Many types of column chromatography are available based on the different
328 stationary phases, such as adsorption chromatography, ion-exchange chromatography, affinity
329 chromatography and size exclusion chromatography. The selection of column type depends on
330 the properties of the target components to be separated. Adsorption chromatography is
331 commonly used for the separation of curcumin, in which the separation is based on different
332 adsorption properties of the compounds on the stationary phase.

333 Curcumin, DMC, and BDMC have different methoxy substitution pattern on the aromatic ring
334 which results in difference in polarity. Therefore, curcumin could be separated from crude
335 curcumin according to the difference in the interactions between curcuminoids and the
336 stationary phase. Silica gel and resin are the most common stationary phases for column
337 chromatography to separate curcumin from curcuminoids. Existed studies suggested that
338 column adsorption chromatography is an effective method for large-scale production of high-
339 purity individual curcuminoids (Jayaprakasha et al., 2002; Revathy et al., 2011; Sahne et al.,
340 2017; Z. Yang et al., 2015). For instance, Revathy et al. (2011) reported silica gel-based
341 adsorption chromatography method for the separation of curcumin, DMC and BDMC with
342 chloroform/methanol as the mobile phase. Using this method, 906.4 mg curcumin, 597.5 mg
343 DMC and 390.5 mg BDMC were obtained from 5 g extracts with a purity of 84%, 86% and
344 80.6%, respectively. In the study conducted by Yang et al. (2015), curcumin, DMC, and BDMC
345 were obtained at high purity of 93.2%, 92.8%, and 88.2% with recoveries of 76.2%, 73.1%, and
346 68.0%, respectively, using resin (a blend of polyamide-6 and poly (styrene-divinyl benzene)
347 (PA-PS-DVB)) as stationary phase. However, column chromatographic techniques are tedious,
348 require large quantity of solvents and are not reproducible. To overcome such
349 challenges, hyphenated techniques (combination of two or more techniques into one integrated
350 technique) were developed for the rapid separation and partial identification of natural products.

351 Moreover, hyphenated techniques could improve the resolution and separation time, and
352 represents a practical approach to resolve problems caused by peak overlap. For instance,
353 Jayaprakasha et al. (2013) established a pseudo two-dimensional liquid flash chromatography
354 to separate curcumin, DMC, BDMC and dihydro bisdemethoxy curcumin (DHBDMC) from
355 turmeric oleoresin using silica and diol columns in series with methanol/chloroform as mobile
356 phase. The purity of isolated curcuminoids was in the 92.4%-95.45% range, as determined by
357 the combined quantitative method (qNMR).

358 3.2. Semi-preparative high performance liquid chromatography (semi-prep HPLC)

359 Semi-prep HPLC is one of the most efficient and widely accept technologies used for the
360 isolation and purification of natural compounds, pharmaceuticals and other products. While it
361 is relatively more expensive and more complex for operators than conventional liquid
362 chromatography. This method takes advantage of high performance separation, online detection,
363 automatic control, high recovery and good reproducibility (Yao et al., 2008; Feng et al., 2011).
364 The compounds of the samples mixture are separated from each other due to their different
365 degrees of interaction (such as hydrophobic and ionic) with the absorbent material. Generally,
366 C₁₈-based column is the most frequently used column for isolation of curcumin and its
367 derivatives DMC and BDMC, and is based on hydrophobic interaction.

368 To obtain curcumin with high purity, the optimum conditions (stationary phase, mobile phase,
369 flow rate, injection volume, and concentration of sample) for good resolution in semi-prep
370 HPLC need to be optimized. However, it was found that the optimal conditions established at
371 analytical scale could be transferred to a preparative one (Mollayi et al., 2015; Owczarek et al.,
372 2017). For instance, Mollayi et al. (2015) optimized the analytical HPLC process, and then
373 chose a preparative HPLC column with the same bed length but about 12 times higher than the
374 volume of the analytical column to separate curcumin from turmeric acetone extracts using
375 optimum conditions. They found the purity of obtained curcumin decreased with the increase

376 of concentration of acetone extract. To achieve pure curcumin at high sample loading
377 concentration, recycling prep HPLC (up to five cycles) was used and higher purity (> 99.0%)
378 of curcumin was obtained when the sample concentration up to 6 mg/mL. Several studies
379 suggested semi-prep HPLC method is very feasible and effective as high purity of curcumin
380 could be obtained (Abu-Lafi et al., 2019; Mollayi et al., 2015; G. Xu et al., 2017). Recently,
381 Abu-Lafi et al. (2019) used semi-prep HPLC to obtain high purity curcumin (92%) from
382 turmeric extract using a flow rate of 20 mL/min, 1 mL injection volume with a concentration
383 of 10 mg/mL, using gradient mixture of acetonitrile and water.

384 3.3. High-speed counter-current chromatography (HSCCC)

385 HSCCC is a liquid-liquid partition chromatographic technique, which has been extensively
386 used for the preparative separation of various active compounds from natural products. It is
387 based on partitioning of compounds between two immiscible liquid phases (Wang et al., 2020),
388 using no supporting matrix; the liquid stationary phase is immobilized by centrifugal force,
389 which eliminates the irreversible adsorption of sample onto the solid support (Hou et al., 2010).
390 Each component can be separated according its distribution coefficients during the liquid-liquid
391 extraction and centrifugal distribution process (Pan et al., 2020).

392 HSCCC is a feasible and effective method for separating curcumin, DMC and BDMC, which
393 can produce individual curcuminoids with high purify (>98%) and has potential to be applied
394 for commercial production in the industry. Inoue et al. (2008) performed simple and efficient
395 purification of curumin, DMC and BDMC by HSCCC using an HSCCC-1A prototype model
396 with a two-phase solvent system composed of n-hexane/chloroform/methanol/water
397 (5/10/7.5/2.5, v/v). The peak resolution values between three compounds were 1.7 and 2.1
398 respectively, and 1.1 mg of curcumin, 0.6 mg DMC and 0.9 mg BDMC were separated from 25
399 mg turmeric powder with purity >98%. With the development of HSCCC, a new high-
400 performance counter-current chromatography (HPCCC) equipment with higher separation

401 efficiency has been developed. Recently, Pan et al. (2020) established a HPCCC method to
402 separate curcumin, DMC and BDMC from crude extract employing an optimized two-phase
403 solvent system n-hexane/ethyl acetate/methanol/water (2/3/3/1, v/v). The curcuminoids were
404 successfully separated within 70 min, and 67 mg curcumin, 18 mg DMC and 9.7 mg BDMC
405 with HPLC purity of 98.26%, 97.39% and 98.67% respectively were obtained from 97 mg crude
406 sample in which their purities were 68.56%, 19.01% and 10.32% respectively.

407 3.4. Preparative supercritical fluid chromatography (prep-SFC)

418 Recently, SFC has attracted extensive attention owing to its high efficiency and environment
419 protecting. The principles are similar to those of HPLC, and are based on adsorption and
420 partition chromatography, and uses columns similar to those in HPLC systems. However, SFC
421 typically utilizes supercritical fluid as the mobile phase (Gibitz-Eisath et al., 2018). CO₂ is most
422 frequently used in SFC, which can be easily pressurized and heated to reach its critical points
423 (31°C and 74 bar); moreover, it is inert, nontoxic, readily available, and cheap (Yang et al.,
424 2019).

425 SFC has been successfully applied to both analytical and preparative scale preparation of
426 natural compounds with similar structures. It has been proved to be a green and powerful tool
427 for separation of curcumin from curcuminoids as high purity curcumin, DMC, and BDMC can
428 be obtained rapidly and efficiently after one single step of separation. Sanagi et al. (1993)
429 reported a process for the analysis of curcumin from turmeric using on line coupling of SFE
430 with SFC and found the separation of curcuminoids by SFC was comparable to that by HPLC.
431 Using this approach, a prep-SFC method was established for the rapid separation of the three
432 curcuminoids from the methanol extract of turmeric (Song et al., 2015). This method was
433 performed with supercritical CO₂ containing 8-15% methanol and 10 mM oxalic acid at a flow
434 rate of 80 mL/min and using a Virids BEH OBD column (Waters, 250 mm × 19 mm, 5 μm).
435 Using this process, 20.8 mg curcumin (97.9% purity), 7.0 mg DMC (91.1% purity), and 4.6 mg

436 BDMC (94.8% purity) were obtained after a single step of SFC separation with a mean recovery
437 of 76.6%.

438 3.5. Crystallization

439 Crystallization is one of the most important separation and purification processes in chemical
440 engineering processing industries, including pharmaceutical and food industries. In general,
441 crystallization can be achieved by four different ways: cooling, evaporation, addition of anti-
442 solvents and precipitation; sometimes two of these can be combined for enhanced results
443 (Gomes & Rodrigues, 2020; Tatsukawa et al., 2020). These strategies are aimed to reach super
444 saturation of the solution so that the transition from the liquid phase to solid phase occurs. With
445 the aim to separate curcumin from the crude curcumin (mixture of curcumin, DMC and BDMC)
446 and suppress spontaneous nucleation of undesired DMC and BDMC, selection of solvents with
447 a relatively low solubility for curcumin and highly solubility for DMC and BDMC or using
448 seed prepared with curcumin solid standard are crucial (Ukrainezyk et al., 2016; Horosanskaia
449 et al., 2020).

450 Usually multi-step successive crystallizations are needed to separate curcumin from crude
451 sample to the desired purity. The process conditions, such as cooling rate, seeding, seed
452 polymorph, agitation method and number of crystallization steps, impact the purity of curcumin.
453 In a study conducted by Ukrainezyk et al. (2016), purification of curcumin from commercially
454 crude curcumin by three or four step successive cooling crystallization has been investigated.
455 It was found that slow cooling and seeded crystallization, particularly with the metastable Form
456 II seed, significantly improves the purification of curcumin. Moreover, the number of
457 crystallization steps required to reach a certain purity can be reduced by tuning the
458 crystallization parameters, which significantly increased the overall curcumin yield. At
459 substantially optimal crystallization conditions (metastable Form II seed, ethanol/water (70%
460 v/v) as solvent, magnetic stirring, and cooling rate of 8°C/h), the overall yield after three

461 successive crystallizations was 50%, reaching purity of 99.85%. Recently, Horosanskaia et al.
462 (2020) developed a separation process for isolation of curcumin from crude curcumin within a
463 single crystallization step. The curcumin purity increased from initial content of 67-75% up to
464 99.4% using acetone, acetonitrile and 50/50 (w/w) mixtures of acetone/2-propanol and
465 acetone/acetonitrile as solvents. Total product yields enhanced to 70-79% via addition of water
466 and acetonitrile as anti-solvents at the end of the cooling crystallization process.

467 In order to obtain all three curcuminoids in the pure form at high yield, a combination of
468 crystallization and chromatography has been studied (**Table 2**). For instance, Heffernan et al.
469 (2017) developed a combined purification method (multistep crystallization and further
470 separation by column chromatography of the remaining mother liquors) for isolation of three
471 curcuminoids from commercially available crude curcumin. 100% pure curcumin, 98.6% pure
472 DMC and 98.3% pure BDMC were obtained with a yield of 88.5%, 79.7% and 68.8%,
473 respectively.

474 **4. Applications of curcumin**

475 Curcumin is extensively used in traditional medicine. In recent years, its demand has increased
476 in the pharmaceutical, food and cosmetic industries. Numerous studies have explored the
477 applications of curcumin in cooking, medicine, beauty, and health products (Chattopadhyay et
478 al., 2004; Esatbeyoglu et al., 2012; Friedrich et al., 2015) . In this regard, the applications of
479 curcumin are summarized in the following sections. A schematic diagram showing the different
480 applications is presented in **Fig. 3**.

481 4.1. Curcumin for medicinal purposes

482 Curcumin is historically valuable in medical applications and has been used in traditional
483 medicine as a household remedy (Chattopadhyay et al., 2004). Its use in various medicines is
484 primarily due to its wide range of beneficial biological and pharmacological activities, i.e., anti-
485 inflammatory, anti-oxidant, anti-bacterial, anti-diabetic, anti-cancer, and anti-tumor

486 (Chattopadhyay et al., 2004; Sharma et al., 2005; Yallapu et al., 2015). In addition, safety
487 evaluation studies indicated that curcumin is well tolerated at a high dose without any toxic
488 effects (Chainani-Wu, 2003). For the last few decades, it has increasingly come under the
489 scientific spotlight thanks to these active biological functions and its highly safe nature.

490 Curcumin exhibits therapeutic effects against numerous types of cancer including bone tumor,
491 brain tumors, head and neck, melanoma, colon, colorectal, pancreatic, breast, prostate, ovarian,
492 lung, and oral cancer (Noorafshan & Ashkani-Esfahani, 2013; Rafiee et al., 2019). The anti-
493 cancer mechanisms involve modulation of numerous molecular targets and signaling pathways,
494 such as NF- κ B, STAT3, and Akt/mTOR (Shehzad et al., 2010; Vallianou et al., 2015), which
495 suppress different cellular processes including cancer cell proliferation, invasion, and
496 metastasis. Curcumin is also effective in prevention and treatment of vascular dysfunctions and
497 cardiovascular diseases, such as cardiomyopathy, oxidative heart injury, cardiac hypertrophy
498 and myocardial infarction (Noorafshan & Ashkani-Esfahani, 2013). Its mechanisms of action
499 are mostly related to its anti-inflammatory effects. Moreover, curcumin also offers protective
500 actions against the nervous system, especially the brain, to prevent and treat diseases related to
501 this vital organ such as Alzheimer's and Parkinson's diseases, by exerting anti-oxidant, anti-
502 inflammatory and anti-protein aggregation activities (Noorafshan & Ashkani-Esfahani, 2013;
503 Vajragupta, 2003). In addition, curcumin has been proven to be a hypoglycemic, anti-
504 pathogenic, anti-viral, hepato-, nephron-protective molecule (Mahmood et al., 2015; Rafiee et
505 al., 2019). Curcumin has also been found to enhance wound healing through involvement in
506 tissue remodeling, granulation tissue formation, and collagen deposition, which is attributed to
507 its biochemical effects such as its anti-inflammatory, anti-infectious and anti-oxidant activities
508 (Mahmood et al., 2015).

509 4.2. Curcumin in the food industry

510 Curcumin (E 100) is a dicinnamoylmethane dye authorized for uses as a food additive in the

511 European Community and was approved by the Joint FAO/WHO Expert Committee on Food
512 Additives (JECFA) and the European Community Scientific Committee on Food (SCF).
513 Furthermore, the admissible daily intake (ADI) is 0-3 mg/kg body weight, as established at the
514 61st JECFA in 2004 (Fisher et al., 2003). However, JECFA specifications consider only
515 curcumin extracted from natural source materials but not synthetic curcumin. Therefore, natural
516 curcumin is widely used in the food industry.

517 Traditionally, curcumin has been employed as a natural food coloring agent, which exhibits an
518 attractive bright yellow-orange color and can serve as a substitute for synthetic food colorants.
519 It is commonly used in rice, meat, mustard, pastries, dairy products, and canned fish
520 (Esatbeyoglu et al., 2012) making foods look better. Furthermore, curcumin can act as a natural
521 preservative to increase the shelf-life of the food. It has a strong anti-microbial efficacy against
522 many microorganisms, including *Escherichia coli*, *Staphylococcus aureus*, *Salmonella*
523 *typhimurium*, and *Listeria monocytogenes* (Altunatmaz et al., 2016). It has been proved that
524 curcumin has a good preservation effect on cooked mutton, bread, bean curd and minced meat
525 (Liang et al., 2007; Altunatmaz et al., 2016). Additionally, curcumin is also proposed as a pH-
526 sensitive indicator or sensor for monitoring and giving information on food quality to
527 manufacturers, retailers or consumers as curcumin is highly sensitive toward acid-base actions.
528 In the process of foods spoilage, color changes of sensor can be monitored directly with visual
529 inspection, also the color can be quantitatively measured after canning with color analysis via
530 software. For instance, a curcumin-based sensor for the detection of volatile amines
531 (specifically known as total volatile basic nitrogen, TVBN) was described by Kuswandi et al
532 (2012). The performance of this sensor was successfully tested directly for real-time monitoring
533 of shrimp spoilage in ambient and chiller conditions.

534 4.3. Curcumin in the cosmetic industry

535 Curcumin has been used for several decades in cosmetic industry owing to its anti-oxidant and

536 anti-inflammatory effects. It has shown potential for a wide variety of beauty treatments for the
537 skin, face, hair, lips, and nail care with beneficial actions against ultraviolet light, aging,
538 inflammation, hair loss, lip care and nail-care. Curcumin can be used in cosmetics for skin
539 protection for properties such as anti-aging, anti-wrinkle, sunscreen and moisture retention
540 (Friedrich et al., 2015; Kaur & Saraf, 2011). Curcumin readily undergoes degradation when
541 exposed to various harsh environmental conditions such as infrared and ultraviolet rays,
542 chemical pollution, and other physical stresses, which can prevent oxygen free radical
543 generation and lipid peroxidation, and can then protect skin against these harmful
544 environmental conditions. Notably, curcumin-loaded formulations can enhance its stability and
545 bioavailability to the skin (cellular uptake and penetration behavior) (Coradini et al., 2014;
546 Friedrich et al., 2015). A continuous supply of curcumin enhances the skin beauty and personal
547 care. Moreover, curcumin is proposed as an anti-bacterial and anti-inflammatory agent for
548 treatment of acne vulgaris. In a study conducted by Liu and Huang (2013), skin accumulation
549 and propionibacterium acnes growth inhibition of curcumin-loaded lipid vesicles *in vitro* were
550 evaluated. It was found that curcumin-loaded lipid vesicles could considerably accumulate in
551 the neonate pig skin and inhibit propionibacterium acnes. Furthermore, curcumin-loaded
552 formulations can effectively penetrate into the hair follicles and can be used for topical
553 curcumin delivery of deep into and through the hair follicles (Jung et al., 2006; Konrádsdóttir
554 et al., 2009). Possible dermal applications include treatment of acne, inflammation, and hair
555 growth disorders.

556 **5. Conclusions and perspectives**

557 Curcumin has been widely used in different industries including food, cosmetics and
558 pharmaceuticals due to its beneficial biological activities and highly safe nature. During last
559 decades, many studies related to extraction and purification of curcumin from plant materials
560 has been reported. The main purpose of this review is to comprehensively summarize the

561 various methods for the extraction and purification of curcumin from plant materials, thereby
562 giving researchers and industrial practitioners complete information to obtain curcumin of high
563 quality. Efficient curcumin extraction processes and techniques should require less energy,
564 should use safe solvents, and give high yield. Conventional methods like solvent extraction,
565 Soxhlet extraction, hydro/steam distillation are time consuming, not eco-friendly and have low
566 efficiencies. Therefore, apposite routes for extraction based on novel technologies such as UAE,
567 MAE, EAE, PLE, SWE, SFE and ionic liquids-based extraction have been examined to
568 maximize the extraction efficiency, decrease the use of toxic solvent, as well as reduce the
569 processing time and energy consumption. These novel technologies could be regarded as green
570 technologies. Purification is an important step in the production of curcumin. Conventional
571 techniques (i.e., column chromatography, semi-preparative HPLC) and supplementary modern
572 techniques (i.e., high-speed counter-current chromatography, supercritical fluid
573 chromatography, etc.) have been comprehensively reviewed. The supplementary modern
574 techniques show excellent selectivity and give high product recovery at low cost, within a short
575 span of time. Moreover, these nonconventional techniques are environmentally friendly and
576 safe. While many of these extraction and purification methods work efficiently as small-scale,
577 their application for large-scale extraction and purification of curcumin is limited. The
578 development of highly efficient extraction and purification methods, and optimization of their
579 operating conditions at pilot-scale are vital for scaling up industrial production of curcumin. In
580 the future, more emphasis should be given on the development of large-scale extraction and
581 purification methods of curcumin.

582 The potential applications of curcumin in different industries including food, cosmetics and
583 pharmaceuticals have attracted a growing numbers of research activities on curcumin extraction
584 and purification. There is a large amount of literature investigating biological activities of free
585 and encapsulated curcumin, and their potential commercial use. With the development of

586 techniques to obtain high purity of curcumin and a deeper comprehension of the properties of
587 curcumin, more and more curcumin products will be produced in the future.

588 **Conflicts of interest**

589 The authors declare that they have no conflict of interest.

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Table 1. Extraction methods of curcumin from plants.

Treatment conditions	Extraction yield	Major findings	References
Solvent extraction			
30°C, 1 h, solid to solvent (acetone, ethyl acetone, ethanol, methanol, and isopropanol) ratio of 1:8 (w/v)	2.4%	Different solvents had potential to extract curcumin and extraction with ethanol gave the highest yield.	(Popuri & Pagala, 2013)
30-80°C, 12-24 h, solid to ethanol (70-96% v/v) ratio of 1:8 (w/v), agitation speed 30-70 rpm	1.8%	The ethanol concentration of the solvent mixture played a crucial role in the extraction process efficiency.	(Paulucci et al., 2013)
Soxhlet extraction			
65°C, 2 days, solid to solvent (ethanol) ratio of 1:4 (w/v)	1.25%	Besides curcumin, secondary metabolite constituents were detected in the extracts.	(Dutta, 2015)
78°C, 8 h, solid to solvent (ethanol) ratio of 1:25 (w/v)	1.28%	Soxhlet extraction produced a higher curcumin extraction rate than UAE, but it was carried out at higher temperature for long duration.	(Shirsath et al., 2017)
Ultrasound-assisted extraction (UAE)			
25-55°C, 1 h, solid to solvent (ethanol, methanol, acetone and ethyl acetate) ratio of 1:15-1:55 (w/v), particle size 0.09-0.85 mm, 250 W, 22 kHz	0.92%	The obtained yield under optimized conditions was significantly higher as compared to batch extraction.	(Shirsath et al., 2017)
10 min, solid to solvent (75-95% ethanol) ratio of 1:200 (w/v), 50-70% amplitude, 1-3 s pulsed duration time	1.03%	Pulsed UAE had better efficiency than UAE in the extraction of curcumin.	(M. Li et al., 2014)
Microwave-assisted extraction (MAE)			
methanol (1:1-1:4 w/v) soaking, 4 min, solid to acetone ratio of 1:20 (w/v), 140-420 W, particles screened through sieve 10-40, 2450 MHz	4.98%	MAE showed drastic reduction in time with much better precision, when compared to conventional extraction methods.	(Mandal et al., 2008)
i : 1-7 min dry irradiation (140 W), 5 min extraction, solid to acetone or ethanol ratio of 1:3 (w/v), 60 W or 90 W, particles screened through sieve 120; ii: water or methanol (1:2) soaking for 24 h, 1-7 min wet powder irradiation (270 W or 50 W)	1.90%	In MAE, curcumin extraction rate increased when water as soaking solvent and acetone as extraction solvent.	(Wakte et al., 2011)

0.5-10 min, solid to ethanol (55-95%) ratio of 1:200 (w/v), 40-120 W, 2450 MHz Enzyme-assisted extraction (EAE)	1.01%	MAE had better efficiency than UAE in the extraction of curcumin.	(M. Li et al., 2014)
0-5% (w/w) α -amylase, glucoamylase, a mixture of cellulase and xylanase, pH 4-6, 2.5-10 h of incubation, 4-16 h of extraction, solid to acetone ratio of 1:8 (w/v)	4.1%	α -Amylase and glucoamylase increased the yields of curcumin by 26.04% and 31.83% respectively under optimum conditions as compared with control.	(Kurmudle et al., 2013)
1-5% (w/w) α -amylase and amyloglucosidase, 2-8 h of incubation (65°C), 1-5 h of extraction (25°C), solid to acetone ratio of 1:10 (w/v)	4.1%	The application of α -amylase and amyloglucosidase on turmeric powder showed 4.1% curcumin extraction yield using EAE under optimum conditions.	(Sahne et al., 2016)
particle size 0.180-0.425 mm, 1-5% (w/w) mixture of α -amylase and amyloglucosidase, 2-8 h of incubation (65 °C), 2-24 h of extraction (15-45 °C), solid to carbamate ionic liquid ratio of 1:10-1:50 (w/w) Pressurized liquid extraction (PLE)	5.73%	Use of a mixture of α -amylase and amyloglucosidase enzymes to pretreat turmeric remarkably improved the extraction yield from 3.58% to 5.73%.	(Sahne et al., 2017)
120-160 °C, 10-25 bar, particle size 0.6-2 mm, 6-22 min	3.8%	The changes in porosity and hardness of turmeric were directly related to the amount of extracted curcumin in process optimization.	(Kiamahalleh et al., 2016)
90-250 °C, 5.0 MPa, pH 1-5.5 phosphate-buffered (40-75 g/mL), solvent flow rate of 0.5 mL/min	1.61%	The extraction yields were improved when the pH was adjusted to a very low value.	(Euterpio et al., 2011)
110-150 °C, 100 atm, 1-10 min; 20%-50% ethanol	-	Pilot-scale extraction gave recoveries comparable to those obtained in lab-scale extraction under optimal conditions.	(Kwon & Chung, 2015)
Supercritical fluid extraction (SFE)			
50 °C, 30 MPa, CO ₂ flow rate of 5 mL/min, 60 min static time, 300 min dynamic time, 10% ethanol as modifier	1.46%	1.46 % curcumin yield was obtained using supercritical CO ₂ with 10% ethanol.	(Wakte et al., 2011)
SFE: 313-333 K, 10-35 MPa, CO ₂ flow-rate of 8.6×10^{-3} kg/min, CO ₂ -to-feed ratio of 12.1 (w/v); PLE: 333-353 K, 10-35 MPa, ethanol as extraction solvent	4.3%	Similar curcuminoid yields were obtained by PLE, Soxhlet and solvent extraction, but the extraction time and cost of manufacturing in PLE were less than those in Soxhlet and solvent extraction.	(Osorio-Tobón et al., 2014)
SFE: 333 K, 250 MPa, CO ₂ -to-feed ratio of 2.4 (w/v), 95 min;	-	The integration of SFE, PLE, and supercritical antisolvent processes	(Osorio-

PLE: 333 K, 10 MPa, ethanol-to-feed ratio of 2.4 (w/v), 110 min; SAS: 313 K, 10 MPa, 80 min			was a feasible alternative to obtain more economic products.	Tobón et al., 2016)
Ionic liquids-based extraction				
Room temperature, 10-90 min, solid to [OMIM]Br (0.1-0.5 mol/L) ratio of 1:30 (w/v), UAE (100-250 W)	6.14%	The curcuminoids yield in [OMIM]Br-based UAE was 6.14%, which was higher than that in 85% ethanol-based UAE (4.40%) and 85% ethanol-based heat-reflux extraction (5.12%).	(Xu et al., 2015)	
Room temperature, 10-90 min, solid to carbamate ionic liquid ratio of 1:10-1:50 (w/v), UAE (100-250 W)	5.73%	The curcuminoids yield in carbamate ionic liquid-based EAE was 5.73%, which was higher than that in acetone-based UAE (3.11%)	(Sahne et al., 2017)	
30-80°C, 2-12 min, solid to [OMIM][Br] (0.2–0.7 mol/L) of 1:15-1:60 (w/v), MAE(300 W, 2455 MHz)	5.3%	The effect of [OMIM][Br] on the MAE of curcuminoids was similar to that of ethanol and methanol.	(H. Liang et al., 2017)	

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Table 2. Purification methods of curcumin.

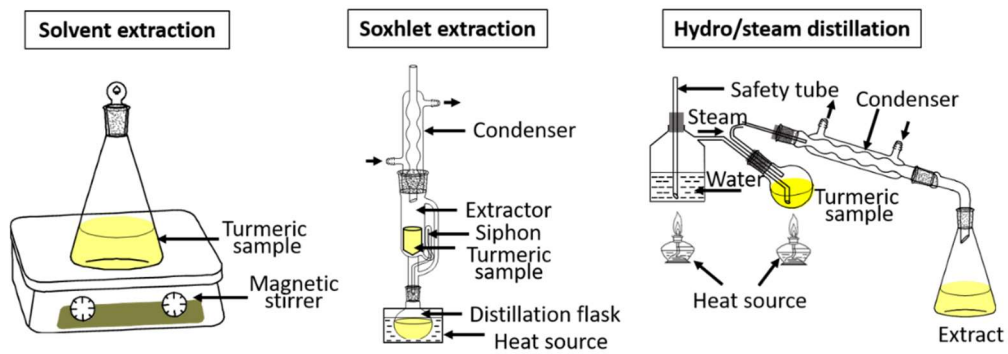
Sources	Material conditions	Operation conditions	Purify	References
Column chromatography (CC)				
acetone extracts	Silica gel column, chloroform/methanol as the mobile phase	Nonisocratic elution mode with increasing polarity after initial elution with chloroform	84%	(Revathy et al., 2011)
oleoresin	Silica and diol columns in series, methanol/chloroform as mobile phase	Nonisocratic elution mode with a stepwise increasing concentration of methanol	95.23%	(Jayaprakasha et al., 2013)
75% ethanol extracts	PA-PS-DVB resin, different concentration of ethanol as mobile phase	pH 6, 20°C, 75%, 85%, and 95% ethanol for eluting curcumin, DMC, and BDMC, respectively	93.2%	(Z. Yang et al., 2015)
Semi-preparative high performance liquid chromatography (semi-prep HPLC)				
acetone extracts	Eurospher C18 column (250×16 mm, 15 µm, 100 Å); methanol-water (50:50 v/v) as mobile phase	Flow rate 10 mL/min, 1 mL injection volume (1 mg/mL)	99.5%	(Mollayi et al., 2015)
ammonium sulfate/ethanol extracts	Kromasil C18 column (250×10mm, 10 µm); CAN-10.5% aqueous acetic acid (45:55 v/v) as mobile phase	Flow rate at 3.5 mL/min, 50 µL injection volume (2 mg/mL)	85.58%	(Xu et al., 2017)
ethanol extracts	CAN and water (1-13 min, 45%-70% (v/v) ACN) as the mobile phase	Flow rate 20 mL/min, 1mL injection volume (10 mg/mL)	92%	(Abu-Lafi et al., 2019)
High-speed counter-current chromatography (HSCCC)				
powder	HSCCC-1A prototype model	Two-phase solvent system: n-hexane/chloroform/methanol/water (5/10/7.5/2.5, v/v)	>98%	(Inoue et al., 2008)
ethanol extracts	Spectrum HSCCC	Two-phase solvent system: n-hexane/ethyl acetate/methanol/water (2/3/3/1, v/v)	98.26 %	(Pan et al., 2020)
Preparative supercritical fluid chromatography (prep-SFC)				
methanol extracts	Virids BEH OBD column (Waters, 250 mm × 19 mm, 5 µm)	Supercritical fluid CO ₂ containing 8-15% methanol at a flow rate of 80 mL/min	97.9%	(Song et al., 2015)

Crystallization

Commercially crude curcumin	metastable Form 2 seed (ethanol/water (70% v/v) as solvents), isopropanol as solvent, three crystallizations	Start/end temperature of cooling step at 70°C/20°C, magnetic stirring, cooling rate at 8°C/h	99.85%	(Ukrainczyk et al., 2016)
Four commercially crude curcumins	Acetone, acetonitrile, 50/50 (w/w) mixtures of acetone/2-propanol and acetone/acetonitrile as solvents, one step crystallization	Start/end temperature of cooling step at 45°C or 60°C/0°C, cooling rate at 10 K/h	90.1-99.4%	(Horosanskaia et al., 2020)
Commercially crude curcumin	Crystallization: metastable Form 2 seed and three crystallizations; CC: silica gel as stationary phase and chloroform/methanol as mobile phase	Crystallization: start/end temperature at 70°C/20°C, cooling rate at 8°C/h; CC: flow rate at 15 mL/min, nonisocratic elution mode with a stepwise increasing methanol concentration	100%	(Heffernan et al., 2017)

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a)

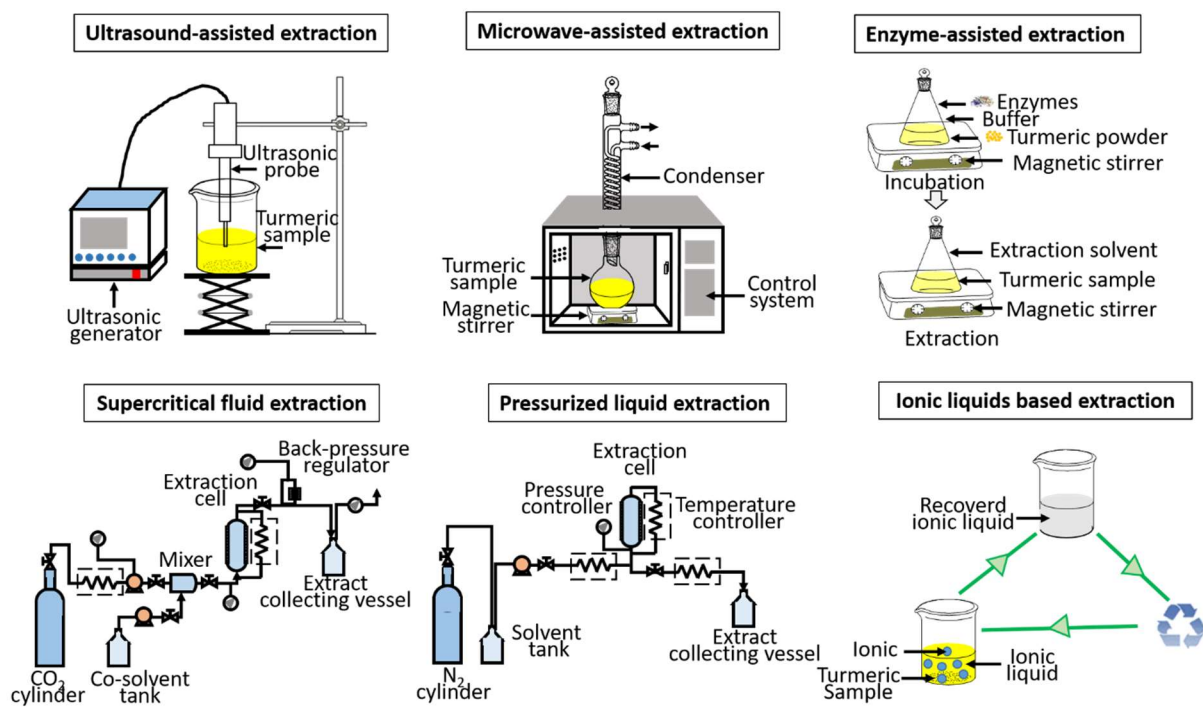


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b)



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Fig. 1. Schematic diagram of a) conventional and b) novel extraction systems.

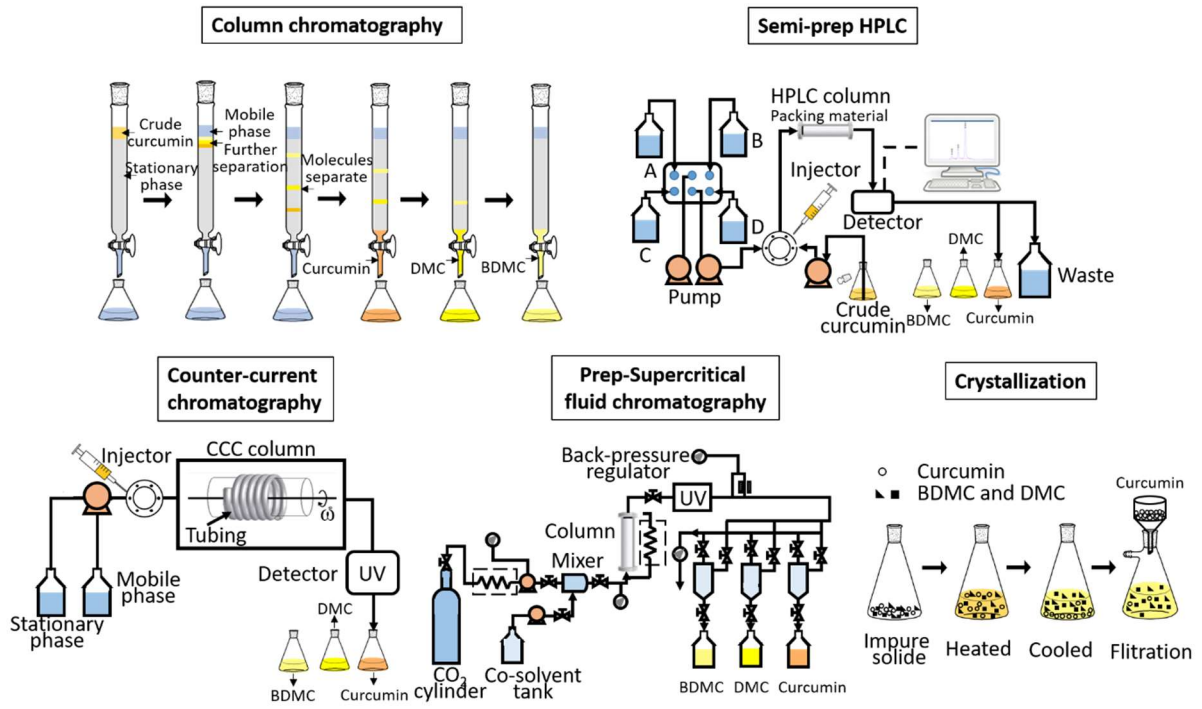


Fig. 2. Schematic diagram of purification systems.

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Pharmaceutical industry

- Against cancer | Modulation of molecular targets and signaling pathways
Anti-oxidant
- Protection nervous system | Anti-inflammatory
Anti-protein aggregation
- Prevention/treatment of cardiovascular diseases | Anti-inflammatory
- Enhance wound healing | Anti-inflammatory
Anti-infectious
Anti-oxidant



Food industry

- Employed as a food colorants | Exhibit bright yellow-orange color
- Act as a natural preservative | Anti-microbial
- Proposed as a pH-sensitive indicator | Sensitive toward acid-base actions



Cosmetic industry

- Against ultraviolet, aging | Prevent oxygen free radical generation
Prevent lipid peroxidation
- Treatment of acne vulgaris | Anti-bacterial
Anti-inflammatory
- Treatment of hair growth disorders | Penetrate into the hair follicles

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Fig. 3. Application of curcumin in different industries

