Variable Secondary Metabolite Profiles Across Cultivars of *Curcuma longa* L. and *C. aromatica* Salisb.

Poonam Kulyal, Satyabrata Acharya[†], Aditya B. Ankari[†], Praveen K. Kokkiripati, Sarada D. Tetali* and Agepati S. Raghavendra*

Department of Plant Sciences, School of Life Sciences, University of Hyderabad, Hyderabad, India

Background: *Curcuma* spp. (Zingiberaceae) are used as a spice and coloring agent. Their rhizomes and essential oils are known for medicinal properties, besides their use in the flavoring and cosmetic industry. Most of these biological activities were attributed to volatile and nonvolatile secondary metabolites present in the rhizomes of *Curcuma* spp. The metabolite variations among the species and even cultivars need to be established for optimized use of *Curcuma* spp.

Objectives: We compared the phytochemical profiles of rhizomes and their essential oils to establish the variability among seven cultivars: five of *Curcuma longa* L. (Alleppey Supreme, Duggirala Red, Prathibha, Salem, Suguna) and two of *C. aromatica* Salisb. (Kasturi Araku, Kasturi Avidi). The GC-MS and LC-MS-based analyses were employed to profile secondary metabolites of these selected cultivars.

Methods: Rhizomes of *Curcuma* spp. were subjected to hydro-distillation to collect essential oil and analyzed by GC-MS. The methanol extracts of fresh rhizomes were subjected to LC-MS analyses. The compounds were identified by using the relevant MS library databases as many compounds as possible.

Results: The essential oil content of the cultivars was in the range of 0.74–1.62%. Several compounds were detected from the essential oils and rhizome extracts by GC-MS and LC-MS, respectively. Of these, 28 compounds (13 from GCMS and 15 from LCMS) were common in all seven cultivars, e.g., α-thujene, and diarylheptanoids like curcumin. Furthermore, a total of 39 new compounds were identified from *C. longa* L. and/or *C. aromatica* Salisb., most of them being cultivar-specific. Of these compounds, 35 were detected by GC-MS analyses of essential oils, 1,2-cyclohexanediol, 1-methyl-4-(1-methylethyl)-, and santolina alcohol, to name a few. The other four compounds were detected by LC-MS of the methanolic extracts of the rhizomes, e.g., kaempferol-3,7-O-dimethyl ether and 5,7,8-trihydroxy-2′,5′-dimethoxy-3′,4′-methylene dioxyisoflavanone.

Abbreviations: CU, curcumin; cvs, cultivars; DMC, demethoxy curcumin; BDMC, bisdemethoxycurcumin.

Conclusions: We identified and recorded the variability in the metabolite profiles of essential oils and whole rhizome extracts from the seven cultivars of *Curcuma longa* L. and *C. aromatica* Salisb. As many as 39 new metabolites were detected in these seven Indian cultivars of *Curcuma* spp. Many of these compounds have health benefits.

Keywords: *Curcuma longa* L., *Curcuma aromatica* Salisb, essential oil, metabolomics, secondary metabolites, GC-MS, LC-MS

INTRODUCTION

Turmeric (*Curcuma longa* L.) is a perennial rhizomatous herb that belongs to the family Zingiberaceae (Prasath et al., 2018). It has been used traditionally in India for its medicinal value and as a spice (Srinivasan et al., 2004; Aggarwal et al., 2007; Esatbeyoglu et al., 2012). In Ayurvedic medicine, turmeric is used internally (as a stomachic, tonic, and blood purifier) or externally (prevention and treatment of skin diseases) (Gounder and Lingamallu, 2012). Turmeric was scientifically validated for several pharmacological benefits, including antioxidant, anti-inflammatory, and chemoprotective properties (Miquel et al., 2002; Krup et al., 2013; Kanase and Khan, 2018; Umar et al., 2020). The rhizomes of turmeric are enriched with several bioactive metabolites, though the attention was mostly on curcuminoids. Besides curcumin (a curcuminoid), the essential oil of *C. longa* L. showed antimicrobial activity and ability to suppress aflatoxins production (Ferreira et al., 2013).

Out of 110 species of genus *Curcuma*, only ~20 species were used so far for phytochemical studies (Nahar and Sarker, 2007). *Curcuma longa* L. is popularly known as turmeric, while *C. aromatica* Salisb. and *C. caesia* Roxb. are known as wild turmeric and black turmeric, respectively. *C. longa* L. and a few other species, including *C. aromatica* Salisb., produce curcumin, a yellow colored curcuminoid. So far, at least 235 compounds, primarily phenolics, terpenoids, and alkaloids, were identified from *Curcuma* spp. (Li et al., 2011). About 70 varieties of *C. longa* L. are cultivated in India (Sasikumar, 2005; Parthasarathy and Chempakam, 2008), but very few are chemically profiled.

The essential oil of *Curcuma* spp. is used in traditional medicine for many ailments (Dosoky and Setzer, 2018). The volatile component of *C. longa*'s rhizome is responsible for its aromatic flavor and odor (Gounder and Lingamallu, 2012). Its essential oil is considered safe for human use (Tisserand and Young, 2013). The oils of *C. longa* L. and *C. aromatica* Salisb. have applications in the food and pharmaceutical industries due to their antioxidant, antibacterial, and anti-inflammatory properties (Dosoky and Setzer, 2018). The essential oil also improved the bioavailability of curcumin, thereby its bioactivity (Shishu and Maheshwari, 2010). Preliminarily clinical trials indicated that the essential oil from *C. longa* L. and *C. aromatica* Salisb. was helpful against cancer, asthma, and other ailments (Cheng et al., 1999; Joshi et al., 2003; Li Y. et al., 2009). Thus, there is a need to identify high-yielding cultivars containing curcuminoids and essential oil.

Since the pharmacological properties of *Curcuma* spp. are dependent on their chemical profiles, studies on the chemical constituents of turmeric/wild turmeric and their essential oils gained significance. Thin-layer chromatography (TLC) is one of the methods employed to quantify curcumin (Setyaningsih et al., 2016) and other curcuminoids (Phattanawasin et al., 2009) in *Curcuma longa* L. A few different techniques used were HPTLC (Pathania et al., 2006; Paramasivam et al., 2009), nuclear magnetic resonance (NMR) spectroscopy (Li W. et al., 2009), and the HPLC method (Kulyal et al., 2016).

Our present study on metabolite profiles would pave the way for metabolomics by providing the identity of several metabolites. Metabolomics is a practical approach for the comprehensive profiling and comparison of metabolites in plant systems (De Vos et al., 2007). It is crucial for quality evaluation and scientific validation of medicinal plants and their products (Mukherjee et al., 2016). Mainly information on secondary metabolites of medicinal plants/spices is of great importance in health, food, and nutrition sectors, due to the antioxidant nature, color, or flavor of these secondary compounds (Beekwilder et al., 2005; Dixon et al., 2006; Hall, 2006). The quality of turmeric and other spices depends on factors, such as cultivation, collection, storage, milling, and processing, apart from genetics and adulteration issues. Therefore, metabolomics provides a practical approach for quality control (Mukherjee et al., 2016; Tetali et al., 2021).

Over the past decade, several methods suitable for large-scale analysis of metabolites in plant extracts were developed (Dixon et al., 2006; Hall, 2006). However, to date, no single analytical method can successfully detect the entire metabolome of higher plants, especially of medicinal and aromatic plants, as they are highly rich in chemically diverse metabolites (Tetali et al., 2021). The GC-MS and LC-MS techniques mutually complement each other in unraveling secondary metabolomes comprising a wide range of volatile and nonvolatile compounds. These compounds belonged to terpenes, phenolic acids, phenylpropanoids, saponins, alkaloids, polyamines, and their derivatives (Huhman and Sumner, 2002; Moco et al., 2006).

Essential oils from different *Curcuma* species, including *C. longa* L. and *C. aromatica* Salisb, were studied for their chemical constituents (Choudhury et al., 1996; Angel et al., 2014; Nampoothiri et al., 2015; Dosoky and Setzer, 2018) to establish their variability. Variation in the volatile compositions of *Curcuma* spp. such as *C. longa* L. and *C. zedoaria*, was done using GC-MS (Dosoky et al., 2019). A combination of GC-MS and LC-MS techniques was used for metabolite analysis of *C. domestica* L. (*C. longa* L.) (Herebian et al., 2009). In the present study, the volatile (essential oil) and nonvolatile (total extract) components of the fresh rhizome of the seven cultivars of *Curcuma* spp. were analyzed by the GC-MS and LC-MS techniques. The present study is the first report revealing such detailed

TABLE 1 | Essential oil content and total number of compounds detected by GC-MS in the rhizomes of *Curcuma* species.

Sl. No.	Cultivar (species)	Essential oil (%)	Identified (Reported in *Curcuma* spp. or another plant species)	Unidentified	
				Unknown	Not reported from any plant species
1	Alleppey Supreme (*C. longa* L.)	1.42	31	58	111
2	Duggirala Red (*C. longa* L.)	0.74	36	56	108
3	Prathibha (*C. longa* L.)	1.20	44	60	96
4	Salem (*C. longa* L.)	1.00	30	39	131
5	Suguna (*C. longa* L.)	0.80	35	51	114
6	Kasturi Araku (*C. aromatica* Salisb.)	0.78	29	64	107
7	Kasturi Avidi (*C. aromatica* Salisb.)	1.62	31	60	109

metabolite profiles of the selected cultivars to the best of our knowledge. These cultivars, except Alleppey Supreme, are typically cultivated in Telangana and Andhra Pradesh, and these states are among the largest producers of turmeric in India (Parthasarathy and Chempakam, 2008).

Most of the studies worldwide on *Curcuma* spp., for their curative properties, were with *C. longa* L., followed by *C. aromatica* Salisb, *C. aeruginosa* Roxb. (Simoh and Zainal, 2015), and *C. kwangsiensis* S. K. Lee & C. F. Liang (Zeng et al., 2009). Several cultivars exist within these species, which vary in their chemical profiles. The present article is the first attempt to characterize both volatile (essential oil) and nonvolatile (crude extract) components of fresh rhizomes of seven cultivars of *Curcuma* spp. by the GC-MS and LC-MS techniques. Our results using GC-MS and LC-MS analyses revealed high variability in their metabolite profiles of seven cultivars of genus *Curcuma*. We emphasize that such an approach could be exploited to distinguish cultivars for a specific application based on their metabolite profile.

MATERIALS AND METHODS

Materials and Reagents
LC-MS grade methanol, water, and acetonitrile were purchased from Fisher Scientific (Pittsburgh, PA, United States). Ammonium formate, formic acid, 4-fluoro-4'-hydroxy benzophenone (97%), and *n*-hexane were from Sigma-Aldrich, India. Anhydrous sodium sulfate (99.99%) was from Merck Millipore, India.

Fresh rhizomes of four cultivars of *Curcuma longa* L. (Duggirala Red, Prathibha, Salem, and Suguna) and two cultivars of *C. aromatica* Salisb. (Kasturi Araku and Kasturi Avidi) were collected from Turmeric Research Station, Kammarpally, Telangana State, India. Alleppey Supreme cultivar of *C. longa* L. was from the Indian Institute of Spices Research, Marikunnu (IISR) Kozhikode, Kerala, India. The mature rhizome samples were collected during the postharvest

season of turmeric (May–Jun) in 2011 and 2012 and cryopreserved at −80°C until extraction and analysis.

Isolation of Essential Oil by Hydrodistillation for GC-MS Analysis
50 g each of fresh turmeric rhizome of five cultivars of *C. longa* L. cvs. Alleppey Supreme, Duggirala Red, Prathibha, Salem, Suguna, and two cultivars of *C. aromatica* Salisb. cvs. Kasturi Araku and Kasturi Avidi were taken out from a −80°C freezer, made into pieces, and ground in a pestle with a mortar to a fine powder under liquid nitrogen. The powder was subjected to hydrodistillation in a Clevenger-type apparatus for 7 h. The essential oil obtained after distillation was dried over anhydrous sodium sulfate and kept at −80°C until GC-MS analysis.

GC-MS Running Conditions and Metabolite Identification
The chemical composition of the *Curcuma* spp. essential oil was analyzed by the GC-MS technique using Agilent 7890 A gas chromatograph coupled with a Leco Pegasus HT TOF mass spectrometer equipped with a 29.8 m × 320 μm HP-5MS 5% phenyl methyl siloxane capillary column with 0.25 μm film thickness. The oven temperature was programmed at 65°C for 2 min and then increased from 65 to 90°C at 5°C/min (held for 3 min). Then the temperature was increased from 90 to 103°C (held for 3 min) and from 103 to 150°C (held for 15 min) at 20°C/min and 8°C/min, respectively. The temperature was raised finally from 150 to 280°C at 20°C/min. The injector, interphase, and ion source were maintained at 250°C, 280°C, and 250°C, respectively. The detector voltage was 1500 V. A solvent delay of 2 min was selected. One microliter (diluted with *n*-hexane; 1:10) of essential oil sample was injected into the GC-MS system using split mode (50: 1). Helium was used as a carrier gas at a flow rate of 1 ml/min. GC-MS data were measured at 70 eV; mass scan 40–1000 amu.

The compounds were identified by comparing their mass spectra with the data available in the literature, National
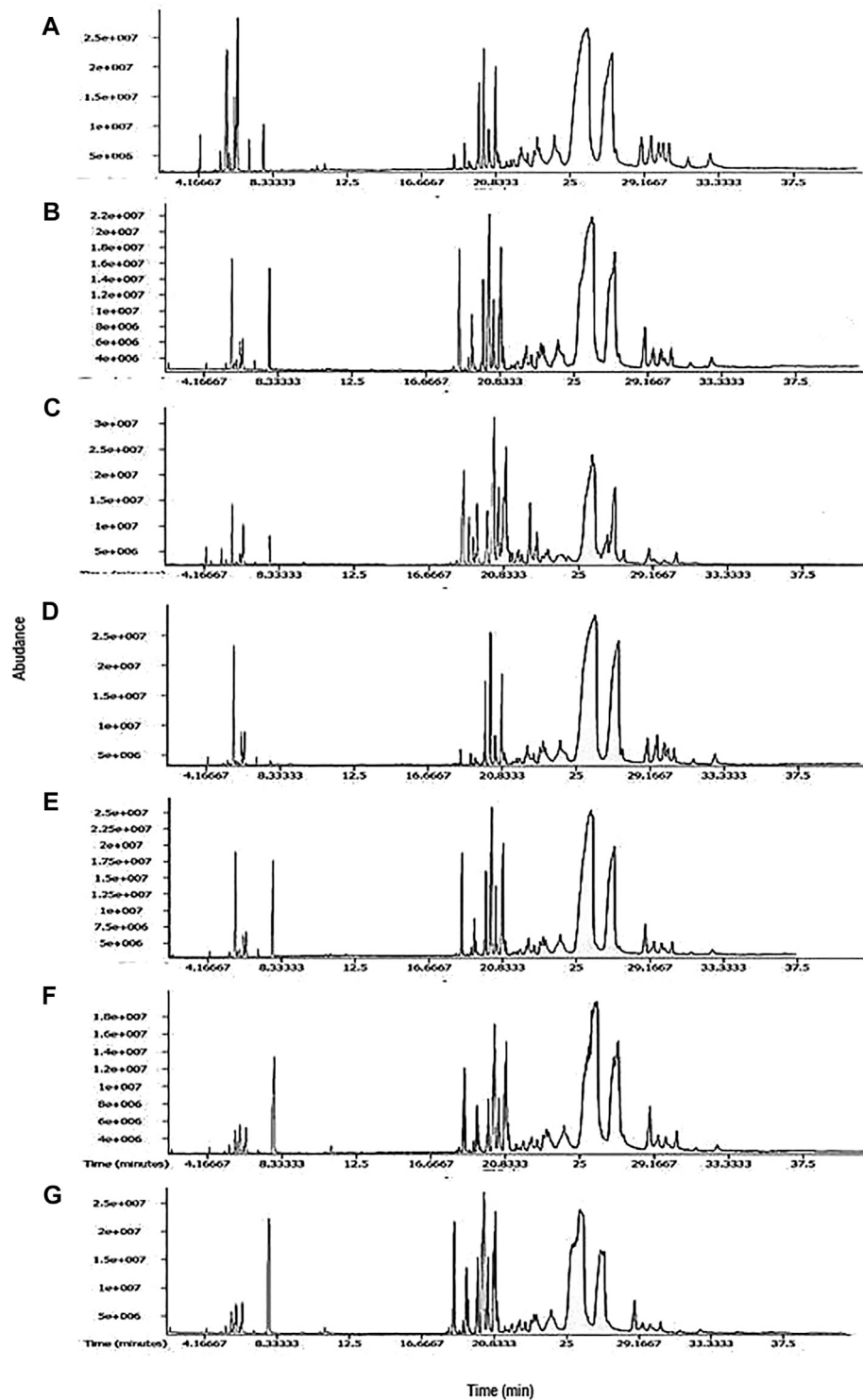
FIGURE 1 | Representative TIC chromatograms from GCMS of essential oil from cultivars **(A)** Alleppey Supreme, **(B)** Duggirala Red, **(C)** Prathibha, **(D)** Salem, **(E)** Suguna of *Curcuma longa* L. and cvs. **(F)** Kasturi Araku, **(G)** Kasturi Avidi of *C. aromatica* Salisb.

Institute of Standards Technology NIST, and Leco-Fiehn Rtx5 libraries. The compounds originated from the GC-MS data file were identified by matching most resembling spectra with the NIST library. Each search produced a hit list of compounds according to match factor or similarity with the library spectra. All the compounds showing similarity more than 70% with the

TABLE 2 | Cultivar-specific compounds identified, in one of the seven cultivars of *Curcuma longa* L. or *C. aromatica* Salisb. by GC-MS in the essential oil from rhizomes. The structures of the compounds (serial numbers from 1 to 23) are given in **Figure 2** (panel numbers: 1–23), and this is the first report of these compounds from the genus *Curcuma* L. These compounds, however, were reported from genus other than *Curcuma* L. The compounds from serial numbers 24 to 41 are already reported in *Curcuma* species. Structures for few compounds (serial numbers 24–30) are given in **Figure 3** (panel numbers: 1–7). Abbreviations used: AS, Alleppey Supreme; DR, Duggirala Red; PR, Prathibha; SA, Salem; SU, Suguna; KAr, Kasturi Araku; KAv, Kasturi Avidi.

Sl. No.	Compound name	Cultivar	RT (Min)	Area/ abundance	Formula	Mass	Mass fragmentations	Class of compound	Reported from plant species	References
1	1,2-Cyclohexanediol, 1-methyl-4-(1-methylethyl)-	AS	6.38	958955880	$C_{10}H_{20}O_2$	172.146	43, 71, 111 154	Monoterpenoid	*Citrus medica* L. Leaf and peel essential oil	Bhuiyan et al. (2009)
2	Trans, trans-Octa-2,4-dienyl acetate	AS	8.22	84981	$C_{10}H_{16}O_2$	168.115	43, 77,79	Dienyl acetate	*Kaempferia galanga* L. Dried rhizomes	Othman et al. (2006)
3	Phenol, 2-methoxy-3-(2-propenyl)-	AS	17.05	200016	$C_{10}H_{12}O_2$	164.083	77,131 164	Phenolic monoterpenoid	*Dalberga stevensonii* Standl. Wood extracts	Jiang et al. (2018)
4	3-Isopropyl-4-methyl-1-pentyn-3-ol	DR	13.59	805101	$C_9H_{16}O$	140.120	43,97 107	Alcohol constituent	*Anethum sowa* Roxb. ex, Fleming Leaf and stem essential oil	Saleh-e-in et al. (2010)
5	5,9-Tetradecadiyne	DR	19.45	11283632	$C_{14}H_{22}$	190.172	41,105, 147	Unsaturated hydrocarbon	*Ferula vesceritensis* Coss. & Durieu ex Trab. Leaves	Zellagui et al. (2012)
6	Naphthalene, 5-butyl-1,2,3,4-tetrahydro-	DR	20.62	1290163	$C_{14}H_{20}$	188.156	91,145 188	Tetralin Type	*Meconopsis punicea* Maxim. and *M. delavayi* (Franch.) Franch. Ex Prain, essential oil	Yuan et al. (2003)
7	Santolina alcohol	DR	23.63	547909	$C_{10}H_{18}O$	154.135	59,81 121	Tertiary alcohol	*Achillea filipendulina* Lam., aerial part	Sharopov and Setzer (2010)
8	2-Pentanone, 4-mercapto-4-methyl-	PR	5.32	1330293	$C_6H_{12}OS$	132.060	43,55 132	Ketone	*Camellia sinensis* (L.) Kuntze	Kumazawa et al. (2005)
9	8-Methylene-3-oxatricyclo[5.2.0.0(2,4)] nonane-	PR	11.72	25554	$C_9H_{12}O$	136.08	40,79, 92	Hydrocarbon	*Schisandra chinensis* (Turcz.) Baill., essential oil dried fruit	Wang et al. (2005)
10	7-Tetracyclo[6.2.1.0(3.8)0(3.9)] undecanol, 4,4,11,11 tetramethyl-	PR	19.16	21297856	$C_{15}H_{24}O$	220.182	77,119 159	Sesquiterpene alcohol	*Cyperus articulatus* L., essential oil roots/rhizome	Metuge et al. (2014)
11	Bicyclo(2.2.1)hept-2-ene, 2,3-dimethyl-	PR	19.41	23461594	C_9H_{14}	122.109	79,94 122	Cyclic hydrocarbon	*Abies alba* Mill leaf and twig	Yang et al. (2009)
12	1H-3a,7-methanoazulene, 2,3,4,7,8,8a-hexahydro-3,6,8,8-tetramethyl-, [3R-(3à,3aá,7á,8aà)]-	PR	19.69	1483176	$C_{15}H_{24}$	204.187	93,119 161	Sesquiterpene	*Lindera aggregata* (Sims) Kosterm., essential oil	Hong (2011)
13	Cholesta-8,24-dien-3-ol, 4-methyl-, (3á,4à)-	PR	21.56	84686714	$C_{28}H_{46}O$	398.354	69,105 119	Triterpenoid	*Parkia speciosa* Hassk. seed	Salman et al. (2006)
14	4-Ethylphenethylamine	PR	25.88	507899185	$C_{10}H_{15}N$	149.120	63,120	Amine	*Psidium guajava* L. stem bark essential oil	Fasola et al. (2011)
15	Cyclohexanol, 2-methyl-5-(1-methylethenyl)-	PR	26.57	3965291	$C_{10}H_{17}O$	154.135	67,107 136	Monoterpenoid	*Mentha spicata* L. aerial parts	Mohammed et al. (2017)
16	Cyclohexane, 1,2-dimethyl-3,5-bis(1-methylethenyl)-	PR	26.59	26170712	$C_{14}H_{24}$	192.187	107,149	Monoterpenoid	*Rhanterium adpressum* Coss. & Durieu Aerial parts	Kala et al. (2009)
17	5,8,11,14-Eicosatetraenoic acid, phenylmethyl ester, (all-Z)-	SA	5.39	15244294	$C_{27}H_{38}O_2$	394.287	67,91 205	Mster	*Petiveria alliacea* L., whole plant	Sathiyabalan et al. (2014)
18	11-Dodecen-2-one	SA	36.83	511982	$C_{12}H_{22}O$	182.167	43,124 182	Ketone	*Ficus hispida* L. f Fresh male and female receptive figs, leaves	Song et al. (2001)
19	E-11-Tetradecenoic acid	SA	37.15	335669	$C_{14}H_{26}O_2$	226.193	41,55,69	Fatty acid	*Coriandrum sativum* L., leaf oil	Bhuiyan et al. (2009)
20	2-Nonen-4-yn-1-ol, (Z)-	SU	10.68	287984	$C_9H_{14}O$	154.135	41,67	Alcohol	*Alpinia speciosa* (J.C. Wendl.) K. Schum	Ho (2010)

(Continued on following page)

TABLE 2 | (*Continued*) Cultivar-specific compounds identified, in one of the seven cultivars of *Curcuma longa* L. or *C. aromatica* Salisb. by GC-MS in the essential oil from rhizomes. The structures of the compounds (serial numbers from 1 to 23) are given in Figure 2 (panel numbers: 1–23), and this is the first report of these compounds from the genus *Curcuma* L. These compounds, however, were reported from genus other than *Curcuma* L. The compounds from serial numbers 24 to 41 are already reported in *Curcuma* species. Structures for few compounds (serial numbers 24–30) are given in Figure 3 (panel numbers: 1–7). Abbreviations used: AS, Alleppey Supreme; DR, Duggirala Red; PR, Prathibha; SA, Salem; SU, Suguna; KAr, Kasturi Araku; KAv, Kasturi Avidi.

Sl. No.	Compound name	Cultivar	RT (Min)	Area/ abundance	Formula	Mass	Mass fragmentations	Class of compound	Reported from plant species	References
21	3-Cyclohexen-1-one, 3,5,5-trimethyl-	SU	21.81	10709364	$C_9H_{14}O$	138.104	95, 138 96, 138	Cyclohexenone	Seeds and leaves *Crocus sativus* L. Dried saffron	D'Auria et al. (2006)
22	6,10-Dodecadien-1-yn-3-ol, 3,7,11-trimethyl-	SU	23.27	18320904	$C_{15}H_{24}O$	220.182	41,67, 95, 138	Sesquiterpenoid	*Hiptage benghalensis* (L.) Kurz, leaves	Venkataramani and Chinnagounder (2012)
23	3-Octen-5-yne, 2,7-dimethyl-, (Z)-	KAv	7.91	132889991	$C_{10}H_{16}$	136.125	93, 121, 136	Monoterpene	*Litsea glutinosa* (Lour.) C.B. Rob Fruit oil	Chowdhury et al. (2008b)
24	Aromadendrene	PR	21.68	32839807	$C_{15}H_{24}$	204.187	41,67,161	Hydrocarbon	*Curcuma purpurascens* Blume, rhizome, essential oil	Hong et al. (2014)
25	Isoborneol	PR	10.16	931077	$C_{10}H_{18}O$	154.135	41,67,95	Monoterpenoid	*Curcuma aromatica* Salisb, rhizome Essential oil	Sasikumar (2005)
26	β-Elemene	PR	17.87	8265459	$C_{15}H_{24}$	204.187	41,67193	Sesquiterpene	*Curcuma longa* L., rhizome Essential oil	Ma and Gang (2006)
27	α-Santalene	PR	19.15	167463111	$C_{15}H_{24}$	204.187	41,94, 122	Sesquiterpene	*Curcuma longa* L., rhizome Essential oil	Chowdhury et al. (2008a)
28	2-Tridecanone	PR	36.82	145399		198.198	43,57	Ketone	*Curcuma albiflora* Thwaites, rhizome Essential oil	Herath et al. (2017)
29	Nonanoic acid	SU	37.82	1054190	$C_9H_{18}O2$	158.1307	41,60,129	Fatty acid	*Curcuma longa* L., rhizome Essential oil	Nieman et al. (2012)
30	Eucalyptol	KAr	6.34	73923505	$C_{10}H_{18}O$	154.135	51,71, 139	Monoterpene	*Curcuma longa* L., rhizome Essential oil	Chowdhury et al. (2008a)
31	Carvacrol	AS	15.46	800060	$C_{10}H_{14}O$	150.104	91, 135	Monoterpene	*Curcuma longa* L., rhizome, essential oil	Awasthi and Dixit (2009)
32	endo-Borneol	PR	25.95	762477	$C_{10}H_{18}O$	154.135	95, 140	Monoterpene	*Curcuma longa* L., rhizome Essential oil	Chowdhury et al. (2008a)
33	1,3,5-Cycloheptatriene, 3,7,7-trimethyl-	KAv	22.26	44959671	$C_{10}H_{14}$	134.109.120	41,91,119	Cyclic hydrocarbon	*Curcuma longa* L., rhizome Essential oil	Chowdhury et al. (2008a)
34	p-Cymen-8-ol	KAr	11.08	28783214	$C_{10}H_{14}O$	150.104	51,91, 135	Monoterpenoid	*Curcuma longa* L., rhizome Essential oil	Chowdhury et al. (2008a)
35	Camphor	PR	9.68	7985363	$C_{10}H_{16}O$	152.120	41,95,152	Terpenoid ketone	*Curcuma longa* L., rhizome Essential oil	Leela et al. (2002)
36	α-Bisabolol	PR	22.60	26108003	$C_{15}H_{26}O$	222.198	41,69, 119	Sesquiterpenoid	*Curcuma longa* L., rhizome Essential oil	Chowdhury et al. (2008a)
37	α-Elemenone	PR	22.99	5795701	$C_{15}H_{22}O$	218.167	67,119, 216	Sesquiterpene	*Curcuma longa* L., rhizome Essential oil	Singh et al. (2010)
38	Caryophyllene oxide	PR	21.85	84236617	$C_{15}H_{24}O$	220.182	21,96,138	Sesquiterpenoid oxide	*Curcuma longa* L., rhizome Essential oil	Chowdhury et al. (2008a)
39	Citral	KAr	10.81	4942325	$C_{10}H_{16}O$	152.120	69,119	Monoterpene	*Curcuma longa* L., rhizome Essential oil	Chowdhury et al. (2008a)
40	Neoisolongifolene, 8,9-dehydro-	KAr	20.92	956644398	$C_{15}H_{24}$	204.187	44,131, 187	Bicyclic hydrocarbon	*Curcuma longa* L., rhizome Essential oil	Chowdhury et al. (2008a)
41	Sabinene hydrate	KAv	19.81	30005835	$C_{10}H_{18}O$	154.135	79,93,121	Monoterpene	*Zingiber Officinale* Roscoe, rhizome essential oil	Koo and Gang (2012)
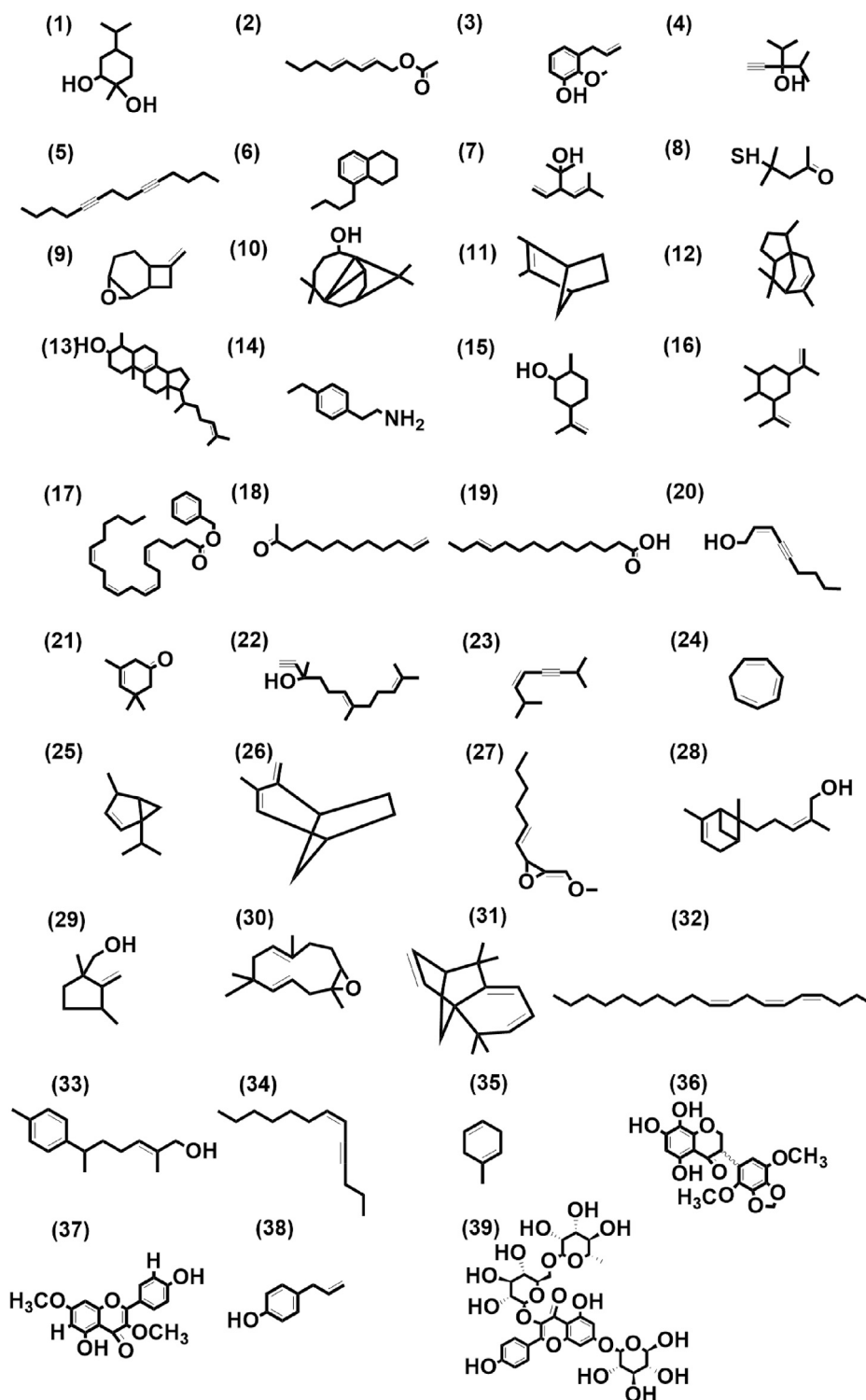
FIGURE 2 | Structures of first-time reported (total 39) from the genus *Curcuma*, identified from cultivars of *Curcuma longa* L. and *C. aromatica* Salisb. detected in essential oil (panel numbers 1–23 and 24–35 corresponding to serial numbers 1–23 and 1–12 of **Tables 2**, **3** respectively) and rhizome extracts (panel numbers 36 and 37–39 corresponding to serial numbers 1 and 1–3 of **Tables 6**, **7** respectively) by GC-MS and LC-MS, respectively. Details of all these compounds are given in **Supplementary Tables S3, S4**. (1) 1,2-Cyclohexanediol, 1-methyl-4-(1-methylethyl)-, (2) trans, trans-octa-2,4-dienyl acetate, (3) phenol, 2-methoxy-3-(2-propenyl)-, (4) 3-isopropyl-4-methyl-1-pentyn-3-ol, (5) 5,9-tetradecadiyne, (6) naphthalene, 5-butyl-1,2,3,4-tetrahydro-, (7) santolina alcohol, (8) 2-pentanone, 4-mercapto-4-methyl-, (9) 8-methylene-3-oxatricyclo[5.2.0.0(2,4)]nonane, (10) 7-tetracyclo[6.2.1.0(3.8)0(3.9)]undecanol, 4,4,11,11 tetramethyl-, (11) bicyclo(2.2.1)hept-

(Continued)

NIST library were selected by the software (Software: Version 4.22 optimized for Pegasus®). Software searches (identifies) compound from their mass spectra and includes MS interpretation programs for analyzing mass spectra based on chemical structure, molecular formula, isotopic pattern, etc. The similarity of 70% or above between the m/z values of the compound detected in the respective cultivar and the MS-libraries' mass fragmentation pattern was considered as identification. Furthermore, mass spectra of all compounds were also matched with ranges available as per their CAS number. Compounds for which the CAS number was not generated, the PubChem CID was used. Compounds below the similarity level of 70% were not considered and grouped as unknown. The data obtained with the samples collected in 2012 are presented in this article.

Preparation of Rhizome Extracts for LC-MS Analysis

Samples for LC-MS analysis were prepared by grinding the fresh rhizome to a fine powder in a mortar and pestle under liquid nitrogen. 1 g of the rhizome powder was suspended in 2 ml of MeOH (LC-MS grade). The samples were sonicated for 30 min and centrifuged for 25 min at 1500 rpm, and the supernatants were separated by filtering through a 0.45-μm Nylon filter disk. These extracts were freshly prepared for the analysis. A 200 μl aliquot of the extract was diluted quantitatively with internal standard (IS) 200 μl 4-fluoro-4′-hydroxy benzophenone solution. It was prepared freshly for each analysis by dissolving in methanol for a final concentration of 0.58 mg/ml. The samples were subjected to LC-MS analysis for the complete metabolite profile. The data obtained with the samples collected in 2012 were presented in this article.

LC-MS/MS Conditions and Metabolite Identification

LC-MS analyses of the crude extract of fresh rhizome of *Curcuma* spp. were performed according to Jiang et al. (2006) using Agilent 6520 Accurate Q-TOF (Agilent Santa Clara, CA), and the column used was Zorbax Eclipse XDB-C 18, 4.6 × 50 mm, 1.8 μ; Mobile phase: A) buffer (5 mM ammonium formate, 0.1% formic acid, in deionized and distilled H_2O) and B) acetonitrile; gradient (in buffer A): 0–2 min, 5% B; 2–57 min, 5–100% B; 57–60 min, 100% B; 60–65 min, 100–5% B; flow rate: 0.25 ml/min; temperature, 40°C; injection volume 5 μl. For the MS detection, Agilent MSD-Trap-SL

was equipped with electrospray ionization (ESI) interface as the ion source. The acquisition parameters for the negative mode were: drying N_2 temperature, 350°C, 8 l/min; nebulizer pressure 40 psi; HV capillary 4000 V; skimmer 65.0 V; mass range measured: 110–1700 m/z; Spray voltage: 4 kV; scan rate 1.4. We analyzed the results in both the positive and the negative ion mode acquired by Agilent TOF/Q-TOF mass spectrometry and full MS scan, in the form of total ion current (TIC) chromatogram, and the metabolites were identified based on their MS/MS spectra and fragmentation rules reported previously (Jiang et al., 2006).

RESULTS

Essential Oil Content

The oil was obtained by hydro-distillation, in a Clevenger-type apparatus, of the fresh rhizomes of five cultivars (Alleppey Supreme, Duggirala Red, Prathibha, Salem, and Suguna) of *Curcuma longa* L. and two cultivars (Kasturi Araku and Kasturi Avidi) of *C. aromatica* Salisb. The yield of essential oil from the seven cultivars was in the range of 0.74–1.62% on a fresh weight basis, with the highest yield of 1.62% in cv. Kasturi Avidi (*C. aromatica* Salisb.) followed by cv. Alleppey Supreme (*C. longa* L.) with an amount of 1.42% and the lowest yield of 0.74% in cv. Duggirala Red (*C. longa* L.). The essential oil yields from the other five rhizomes were in between these values (**Table 1**). The oil yields of *C. longa* L. varieties were higher than those of *C. aromatica* Salisb.

GC-MS Analysis of Essential Oil

Essential oils of seven cultivars of *Curcuma* spp. were subjected to GC-MS analysis, and the results from one of such studies for each cultivar are presented in this article. The representative TIC chromatograms of these cultivars are shown in **Figure 1**. Several compounds were detected in each cultivar's essential oil (**Table 1**). Only a few of the identified compounds were confirmed based on their match with the compound profiles found in the NIST databases and Leco-Fiehn Rtx5 library. Up to 44 compounds were identified from the five cvs. of *C. longa* L. and 31 compounds from two cvs. of *C. aromatica* Salisb. (**Table 1**). Altogether 80 compounds were grouped into three categories: cultivar-specific (41), present in more than one cultivar (26), and common in all seven cultivars (13).

These 41 cultivar-specific compounds were detected in the essential oil of one of the cultivars of *C. longa* L. or *C. aromatica* Salisb. (**Table 2**). The essential oil of *C. longa* L. cv. Prathibha had the highest number of cultivar-specific compounds, whereas *C.*

TABLE 3 | Compounds detected in more than one cultivar of *C. longa* L. and *C. aromatica* Salisb. identified by GCMS in the essential oil from rhizomes. The structures of the compounds from serial numbers 1–12 are given in **Figure 2** (panel numbers: 24–35), and the compounds with Sl.No. 13–18 are shown in **Figure 3**, with corresponding panel numbers: 8–13 respectively. Abbreviations used: AS, Alleppey Supreme; DR, Duggirala Red; PR, Prathibha; SA, Salem; SU, Suguna; KAr, Kasturi Araku; KAv, Kasturi Avidi.

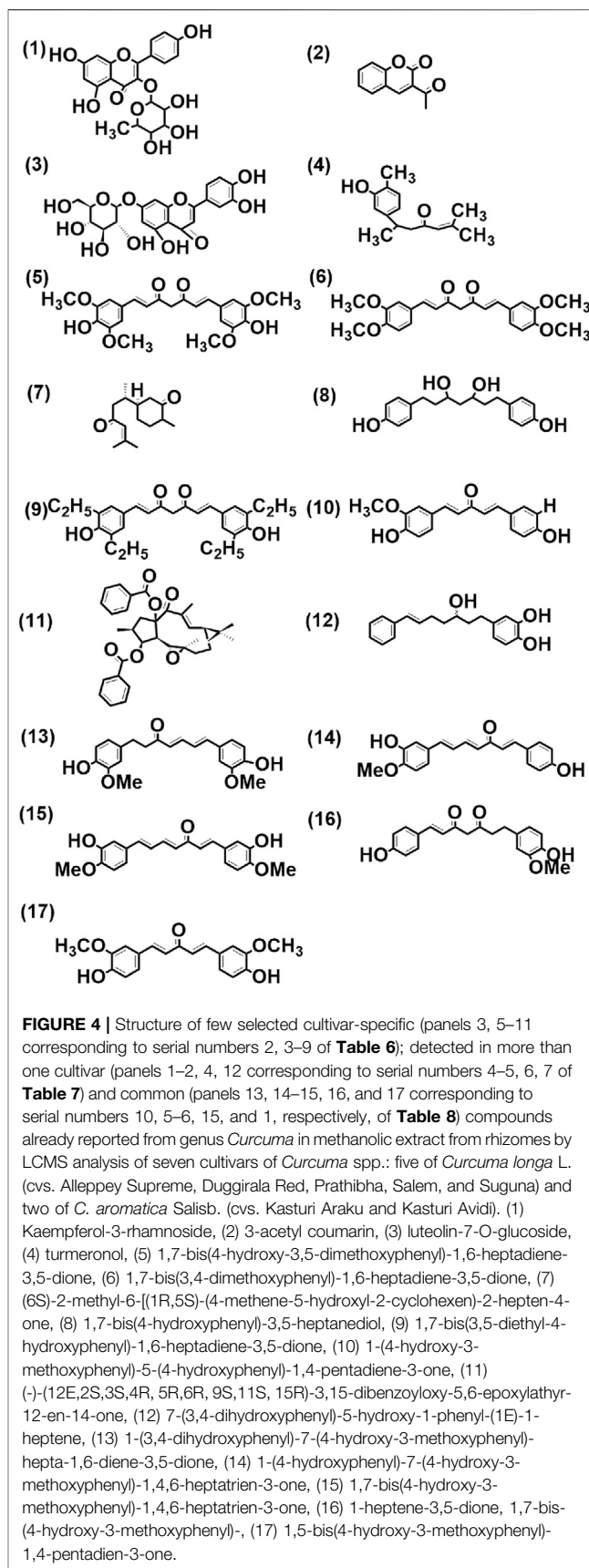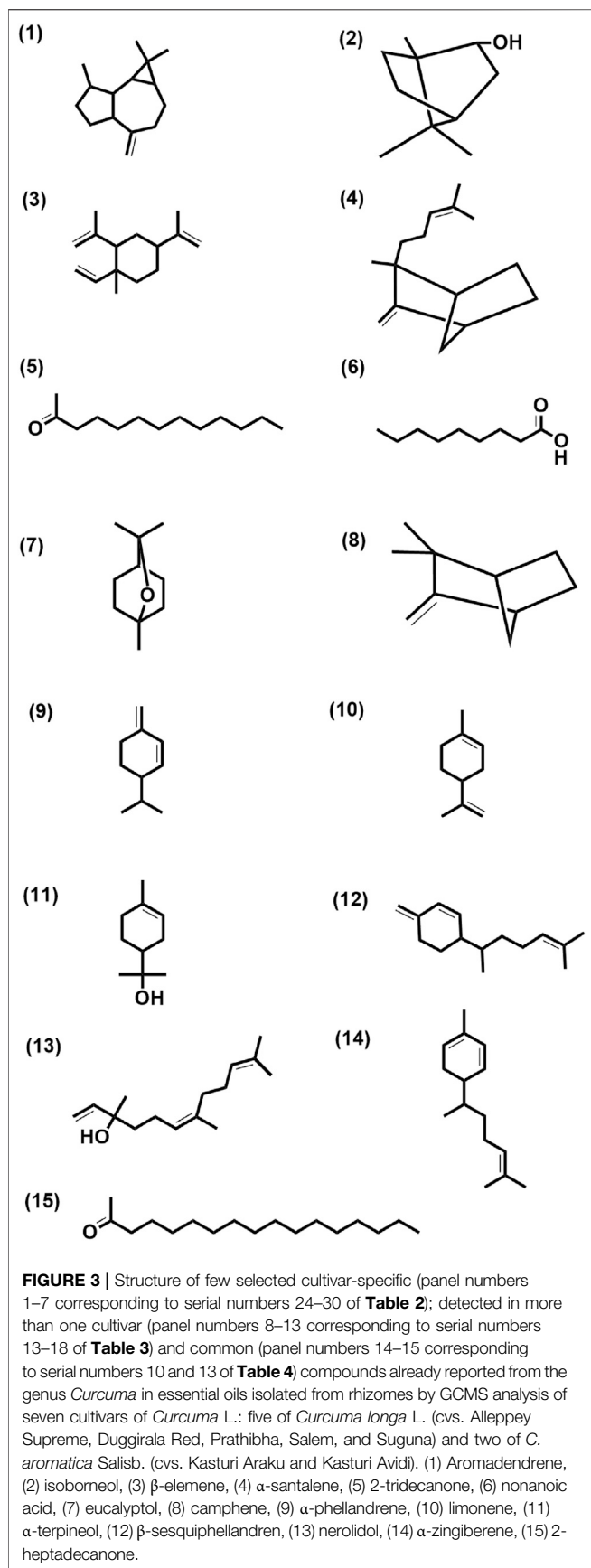| Sl No.	Compound name	Cultivar	RT (Min)	Area/ abundance	Formula	Mass	Mass fragment ions	Class of compound	Reported from plant species	References
1	1,3,5-Cycloheptatriene	AS, PR, SA, SU, KAr, KAv	2.16	6243556	C_7H_8	92.0626	65,91	Closed ring organic compound	*Ceropegia woodii* Schltr	Meng et al. (2010)
2	Bicyclo(3.1.0)hexane, 4-methyl-1-(1-methylethyl)-, didehydro deriv	DR, PR, SA, SU	5.70	89775296	$C_{10}H_{16}$	136.1252	41, 77, 93	Monoterpene	*Zingiber Officinale* Roscoe	Tang et al. (2012)
3	Bicyclo(3.2.1)oct-2-ene, 3-methyl-4-methylene-	DR, SU, KAv	9.35	559996	$C_{10}H_{16}$	134.1096	91, 105, 134	Monoterpene	*Seseli daucifolium* C.B. Clarke	Mohiuddin et al. (2012)
4	Oxirane, 2-(hexyn-1-yl)-3-methoxymethylene-	DR, KAr, KAv	9.75	71555	$C_{10}H_{14}O_2$	166.0994	79, 110	Cyclic ether and epoxide	*Hyptis spicigera* Lam	Ladan et al. (2011)
5	Bergamotol, Z-α-trans-	AS, SA	20.90	39326774	$C_{15}H_{24}O$	220.182	91, 93,119,187	Sesquiterpene alcohol	*Pogostemon deccanensis* (Panigrahi) Press	Kumar et al. (2019)
6	(1,3-Dimethyl-2-methylene-cyclopentyl)-methanol	AS, DR, SA, SU, KAv	21.05	25037989	$C_9H_{16}O$	140.1201	67, 77, 94, 109	alcohol H	*Elsholtzia argyi* H. Lév	Peng and Yang (2005)
7	12-Oxabicyclo[9.1.0]dodeca-3,7-diene, 1,5,5,8-tetramethyl-, [1R-(1R*,3E,7E,11R*)]-	DR, KAr	21.67	21304483	$C_{15}H_{24}O$	220.1827	67, 96, 109, 138	Epoxide	*Eugenia Caryophyllus* (Spreng.) Bullock & S.G. Harrison	Mani and Boominathan (2011)
8	Isolongifolene, 4,5,9,10-dehydro-	AS, DR, SA, SU, KAr	22.10	350003	$C_{15}H_{20}$	200.1565	77, 91, 143, 157, 185	Polycyclic hydrocarbon	*Cymbopogon citratus* (DC.) Stapf	Tajidin (2012)
9	Z,Z,Z-4,6,9-Nonadecatriene	DR, KAv	22.33	169215573	$C_{34}H_{19}$	262.2661	79, 93	Hydrocarbon	*Papaver somniferum* L.	Kumaravel et al. (2019)
10	6-(p-Tolyl)-2-methyl-2-heptenol	AS, SU, KAv	22.98	60406564	$C_{15}H_{22}O$	218.167	91, 119, 202	Aromatic alcohol	*Zingiber officinale* Roscoe	Choudhari and Kareppa (2013)
11	6-Tridecen-4-yne, (Z)-	DR, PR, SU	23.14	153999724	$C_{13}H_{22}$	178.1722	43, 79, 94	Hydrocarbon	*Ambrosia trifida* L.	Wang et al. (2005)
12	1,4-Cyclohexadiene, 1-methyl-	KAr, KAv	23.15	156905042	C_7H_{10}	94.0783	55, 79,94	Aromatic alcohol	*Capsicum annuum* L.	Eggink et al. (2012)
13	Camphene	AS, DR, PR, SU	4.56	930505	$C_{10}H_{16}$	136.125	93, 121	Monoterpene	*Curcuma longa* L.	Chowdhury et al. (2008a)
14	α-Phellandrene	AS, DR, SA, SU, KAr	5.72	2645357306	$C_{10}H_{16}$	136.125	77, 93	Monoterpene	*Curcuma longa* L.	Chowdhury et al. (2008a)
15	Limonene	AS, SU, KAr, KAv	6.27	202198637	$C_{10}H_{16}$	136.125	68, 93	Monoterpene	*Curcuma longa* L.	Singh et al. (2010)
16	α-Terpineol	AS, PR, SA, SU, KAr, KAv	11.25	35019844	$C_{10}H_{18}O$	154.135	59 93, 121	Monoterpenoid	*Curcuma longa* L.	Gopalan et al. (2000)
17	β-Sesquiphellandren	DR, SA, SU, KAv	20.83	962609070	$C_{15}H_{24}$	204.187	68, 79	Sesquiterpene	*Curcuma longa* L.	Chowdhury et al. (2008a)
18	Nerolidol	DR, PR, SA, SU, KAv	21.79	15626126	$C_{15}H_{26}O$	222.198	69, 93	Sesquiterpinol	*Curcuma longa* L.	Awasthi and Dixit (2009)
19	Bicyclo(4.1.0)hept-2-ene, 3,7,7-trimethyl-	DR, KAv	5.63	227551	$C_{10}H_{16}$	136.125	93, 121	Monoterpene	*Curcuma longa* L.	Chowdhury et al. (2008a)
20	α-Terpinene	AS, DR, SA, KAr, KAv	6.00	28366949	$C_{10}H_{16}$	136.125	93, 121, 136	Monoterpene	*Curcuma longa* L.	Chowdhury et al. (2008a)
21	cis-Ocimene	DR, PR, SA, SU, KAr, KAv	6.74	466438	$C_{10}H_{16}$	136.125	41, 93	Monoterpene	*Curcuma longa* L.	Usman et al. (2009)
22	γ-Terpinene	AS, DR, PR, SA, SU, KAr	7.01	26650014	$C_{10}H_{16}$	136.125	93, 119,136	Monoterpene	*Curcuma longa* L.	*Curcuma longa* L. Usman et al. (2009)
23	Linalool	AS, DR, PR, SU	8.15	500594	$C_{10}H_{18}O$	154.135	71, 93, 121	Alcohol	*Curcuma longa* L.	*Curcuma longa* L. Leela et al. (2002)

TABLE 3 | (*Continued*) Compounds detected in more than one cultivar of *C. longa* L. and *C. aromatica* Salisb. identified by GCMS in the essential oil from rhizomes. The structures of the compounds from serial numbers 1–12 are given in Figure 2 (panel numbers: 24–35), and the compounds with Sl.No. 13–18 are shown in Figure 3, with corresponding panel numbers: 8–13 respectively. Abbreviations used: AS, Alleppey Supreme; DR, Duggirala Red; PR, Prathibha; SA, Salem; SU, Suguna; KAr, Kasturi Araku; KAv, Kasturi Avidi.

Sl No.	Compound name	Cultivar	RT (Min)	Area/ abundance	Formula	Mass	Mass fragment ions	Class of compound	Reported from plant species	References
24	Terpinene-4-ol	AS, DR, PR, SA, SU	10.83	2557284	$C_{10}H_{18}O$	154.135	73, 94, 154	Monoterpene	*Curcuma longa* L.	*Curcuma longa* L. Singh et al. (2010)
25	cis-α-Bisabolene	PR, KAr	20.40	11244271	$C_{15}H_{24}$	204.187	67, 93, 161, 204	Sesquiterpene	*Curcuma longa* L.	*Curcuma longa* L. Chowdhury et al. (2008a)
26	Ar-Tumerone	DR, SA, KAv	25.87	328137262	$C_{15}H_{20}O$	216.151	83, 119, 173, 216	Sesquiterpene	*Curcuma longa* L.	*Curcuma longa* L. Chowdhury et al. (2008a)

TABLE 4 | Compounds common in the seven cultivars of *Curcuma* spp detected by GC-MS in essential oil obtained from rhizomes. The structures of the two compounds with serial numbers 10 and 13 are given in **Figure 3** (panel numbers: 14–15 respectively).

Sl No.	Compound name	RT (Min)	Area/abundance	Formula	Mass	Mass fragment ions	Class of compound	Reported from plant species	References
1	α-Thujene	4.13	9407392	$C_{10}H_{16}$	136.125	93, 136	Monoterpenoid	*Curcuma longa* L.	Raina et al. (2005)
2	1s-α-Pinene	4.27	122103688	$C_{10}H_{16}$	136.125	39, 41, 93	Monoterpenoid	*Curcuma longa* L.	Singh et al. (2002)
3	Sabinene	5.05	3901899	$C_{10}H_{16}$	136.125	93, 136	Monoterpenoid	*Curcuma longa* L., leaves	Behura et al. (2002)
4	β or m-Cymene	6.20	338719033	$C_{10}H_{14}$	134.109	65, 91, 119	Aromatic hydrocarbon	*Curcuma longa* L.	Singh et al. (2002)
5	Terpinolene	7.82	225186296	$C_{10}H_{16}$	136.125	93, 121	Monoterpenoid	*Curcuma longa* L.	Leela et al. (2002)
6	trans-α-Bergamotene	18.86	2365810	$C_{15}H_{24}$	204.187	69, 93, 119, 161	Sesquiterpene	*Curcuma longa* L.	Raina et al. (2005)
7	α-Caryophyllene	19.23	6097261	$C_{15}H_{24}$	204.187	93, 121	Sesquiterpene	*Curcuma longa* L., leaves	Behura et al. (2002)
8	trans-β-Farnesene	19.37	211225438	$C_{15}H_{24}$	204.187	69, 93, 133	Sesquiterpene	*Curcuma longa* L.	Singh et al. (2002)
9	Ar-Curcumene	19.88	482956678	$C_{15}H_{22}$	202.172	132, 202	Sesquiterpene	*Curcuma longa* L.	Singh et al. (2002)
10	α-Zingiberene	20.25	1117738917	$C_{15}H_{24}$	204.187	69, 93, 119, 204	Sesquiterpene	*Curcuma longa* L.	Chowdhury et al. (2008a)
11	Tumerone	22.16	67277186	$C_{15}H_{22}O$	218.167	83, 157	Sesquiterpene	*Curcuma longa* L.	Singh et al., 2002)
12	Curlone	27.34	439832546	$C_{15}H_{22}O$	218.167	83, 120, 218	Sesquiterpene	*Curcuma longa* L.	Leela et al. (2002)
13	2-Heptadecanone	39.17	152911	$C_{17}H_{34}O$	254.261	43, 55, 71, 125	Ketone	*Curcuma angustifolia* Roxb	Srivastava et al. (2006)

FIGURE 3 | Structure of few selected cultivar-specific (panel numbers 1–7 corresponding to serial numbers 24–30 of **Table 2**); detected in more than one cultivar (panel numbers 8–13 corresponding to serial numbers 13–18 of **Table 3**) and common (panel numbers 14–15 corresponding to serial numbers 10 and 13 of **Table 4**) compounds already reported from the genus *Curcuma* in essential oils isolated from rhizomes by GCMS analysis of seven cultivars of *Curcuma* L.: five of *Curcuma longa* L. (cvs. Alleppey Supreme, Duggirala Red, Prathibha, Salem, and Suguna) and two of *C. aromatica* Salisb. (cvs. Kasturi Araku and Kasturi Avidi). (1) Aromadendrene, (2) isoborneol, (3) β-elemene, (4) α-santalene, (5) 2-tridecanone, (6) nonanoic acid, (7) eucalyptol, (8) camphene, (9) α-phellandrene, (10) limonene, (11) α-terpineol, (12) β-sesquiphellandren, (13) nerolidol, (14) α-zingiberene, (15) 2-heptadecanone.

FIGURE 4 | Structure of few selected cultivar-specific (panels 3, 5–11 corresponding to serial numbers 2, 3–9 of **Table 6**); detected in more than one cultivar (panels 1–2, 4, 12 corresponding to serial numbers 4–5, 6, 7 of **Table 7**) and common (panels 13, 14–15, 16, and 17 corresponding to serial numbers 10, 5–6, 15, and 1, respectively, of **Table 8**) compounds already reported from genus *Curcuma* in methanolic extract from rhizomes by LCMS analysis of seven cultivars of *Curcuma* spp.: five of *Curcuma longa* L. (cvs. Alleppey Supreme, Duggirala Red, Prathibha, Salem, and Suguna) and two of *C. aromatica* Salisb. (cvs. Kasturi Araku and Kasturi Avidi). (1) Kaempferol-3-rhamnoside, (2) 3-acetyl coumarin, (3) luteolin-7-O-glucoside, (4) turmeronol, (5) 1,7-bis(4-hydroxy-3,5-dimethoxyphenyl)-1,6-heptadiene-3,5-dione, (6) 1,7-bis(3,4-dimethoxyphenyl)-1,6-heptadiene-3,5-dione, (7) (6S)-2-methyl-6-[(1R,5S)-(4-methene-5-hydroxyl-2-cyclohexen)-2-hepten-4-one, (8) 1,7-bis(4-hydroxyphenyl)-3,5-heptanediol, (9) 1,7-bis(3,5-diethyl-4-hydroxyphenyl)-1,6-heptadiene-3,5-dione, (10) 1-(4-hydroxy-3-methoxyphenyl)-5-(4-hydroxyphenyl)-1,4-pentadiene-3-one, (11) (-)-(12E,2S,3S,4R, 5R,6R, 9S,11S, 15R)-3,15-dibenzoyloxy-5,6-epoxylathyr-12-en-14-one, (12) 7-(3,4-dihydroxyphenyl)-5-hydroxy-1-phenyl-(1E)-1-heptene, (13) 1-(3,4-dihydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-hepta-1,6-diene-3,5-dione, (14) 1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-1,4,6-heptatrien-3-one, (15) 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,4,6-heptatrien-3-one, (16) 1-heptene-3,5-dione, 1,7-bis-(4-hydroxy-3-methoxyphenyl)-, (17) 1,5-bis(4-hydroxy-3-methoxyphenyl)-1,4-pentadien-3-one.

TABLE 5 | Total number of compounds detected by LC-MS from the rhizome extract of *C. longa* L. *and C. aromatica* Salisb.

Sl. No.	Cultivar (Species)	Total number of Metabolites detected	Metabolites identified	Unknown Metabolites
1	Alleppey Supreme (*C. longa* L.)	86	43	43
2	Duggirala Red (*C. longa* L.)	107	23	84
3	Prathibha (*C. longa* L.)	60	28	32
4	Salem (*C. longa* L.)	91	28	63
5	Suguna (*C. longa* L.)	96	30	66
6	Kasturi Avidi (*C. aromatica* Salisb.)	90	30	60
7	Kasturi Araku (*C. aromatica* Salisb.)	92	29	63

aromatica Salisb., cv. Kasturi Araku had the least (**Table 2**). Of these, 23 cultivar-specific compounds were reported for the first time from the genus *Curcuma*. The chemical structures of these 23 compounds (**Table 2**, Sl. Nos. 1–23) are presented in **Figure 2** (panels 1–23). In addition to 41 cultivar-specific compounds, 26 compounds were present in more than one cultivar (**Table 3**). Among these, 12 were detected first time in the genus *Curcuma* (**Table 3**, Sl. Nos. 1 to 12; **Figure 2**, panels: 24–35). The remaining 14 were already known in *C. longa* L. A total of 13 compounds were common in all seven cultivars of *C. longa* L. and *C. aromatica* Salisb. (**Table 4**) and the representative structures of two of these compounds are given in **Figure 3** (panel numbers 14–15, corresponding to serial numbers 10 and 13 respectively of **Table 4**). Most of these compounds belong to mono, di, and sesquiterpene. A summary of all 80 compounds identified by GC-MS in the essential oils of the seven cultivars is presented in **Supplementary Table S1**.

LC-MS Analysis of Methanol Extracts

Methanolic extracts of rhizomes from the seven cultivars of *Curcuma* spp. were subjected to LC-MS analysis. The results from one of such analyses for each cultivar are presented in this article. The use of "positive" and "negative" modes of LC-MS was quite helpful. TIC chromatograms of all seven cultivars of *Curcuma longa* L. and *C. aromatica* Salisb. were shown in **Supplementary Figure S1A** for negative mode and **Supplementary Figure S1B** for positive mode.

A typical LC-MS analysis of methanolic extracts from rhizomes of *C. longa* L. cv. Alleppey Supreme revealed the presence of up to 86 compounds. Out of these, 43 were identified, and the remaining 43 compounds remained unknown. The (-) ESI-LC-MS detected 30 known compounds, and the (+) ESI-LC-MS detected 23 known compounds with an overlap of 10 compounds, detected by both negative and positive ion modes. A similar assessment of data was done with all seven cultivars of *Curcuma* spp. (**Table 5**). Altogether 62 compounds were identified, as presented in **Supplementary Table S2**. These compounds were grouped into three categories: cultivar-specific,

detected in more than one cultivar, and common. There were 23 cultivar-specific compounds present in any one cultivar of *C. longa* L. or *C. aromatica* Salisb. (**Table 6**). 24 compounds were present in more than one cultivar of *C. longa* L. and/or *C. aromatica* Salisb. (**Table 7**). The remaining 15 were common in all seven cultivars (**Table 8**). Of these 15 common compounds found in the LC-MS/MS chromatograms, only one was a "Bisabolane" sesquiterpene (Parthasarathy et al., 2009) and all other 14 were diarylheptanoids. These were identified based on the MS/MS spectra reported by Jiang et al. (2006), including curcumin (CU), demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC). Among the other diarylheptanoids, 1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-1,4,6-heptatrien-3-one; 1,5-bis(4-hydroxy-3-methoxyphenyl)-1,4-pentadien-3-one, etc., were common in all the cultivars of *C. longa* L. and *C. aromatica* Salisb. (**Table 8**). The structure of the five common compounds was given in **Figure 4** (panels 13, 14–15, 16, and 17 corresponding to serial numbers 10, 5–6, 15, and 1, respectively, of **Table 8**). In addition to diarylheptanoids, several other classes (phenolic acids, flavonoids, ketonic sesquiterpenes, and fatty acid derivatives) were also detected in the turmeric rhizomes.

Compounds Reported First Time From the Genus Curcuma Using GC-MS and LC-MS Analysis

A total of 39 compounds were detected (**Figure 2**) for the first time from the genus *Curcuma*. Out of these, 35 and 4 compounds were identified respectively in the essential oils and whole rhizome extracts of *C. longa* L. and *C. aromatica* Salisb. by the GC-MS and LC-MS techniques. Details of the compounds, including the class of compound, molecular weight, are given in **Tables 2, 3, 5**, and **6**; structures of all these compounds are shown in **Figure 2** (panels: 1–39). The MS and MS/MS spectra of these compounds are presented in **Supplementary Figure S2** (panels: 1–39). These compounds were reported earlier from plants belonging to any genus other than *Curcuma,* and this is the first report from genus

TABLE 6 | Cultivar-specific compounds identified by LC-MS in the rhizome extracts from one of the seven cultivars of *Curcuma longa* L. and *C. aromatica* Salisb. The structure of the compound with the serial number "1" is given in **Figure 2** (panel number: 36) and compounds with Sl. Nos. 2, 3–9 are given in **Figure 4** with the corresponding panel nos. 3, 5–11, respectively. Abbreviations used: AS, Alleppey Supreme; DR, Duggirala Red; PR, Prathibha; SA, Salem; SU, Suguna; KAr, Kasturi Araku; KAv, Kasturi Avidi.

Sl. No.	Compound name	Cultivar	RT (Min)	Area/ abundance	Formula	Mass (m/z)	Mass fragment ions	Class of compound	Reported from plant species	References
1	Kaempferol-3,7-O-dimethyl ether	AS	12.77	25537	$C_{17}H_{14}O_6$	313.0721 M-H⁻	108; 123; 152; 153 167	Flavonoid	*Lumnitzera racemosa* Willd and *Artemisia vulgaris* L.	Nikolova (2006); DeSouza et al. (2010)
2	Luteolin-7-O-glucoside	AS	42.2	5324	$C_{21}H_{20}O_{11}$	447.2733 M-H	110; 185; 279; 280	Flavonoid	*Curcuma Zedoaria* (Christm.) Roscoe	Mass bank ACCESSION: TY00-0145; Rahmatullah et al. (2012)
3	1,7-Bis(4-hydroxy-3,5-dimethoxyphenyl)-1,6-heptadiene-3,5-dione	PR	32.9	186331	$C_{23}H_{24}O_8$	428.2 M-H	109; 123; 137; 159; 191; 209	Diarylheptanoid	Curcuma longa L.	Nurfina et al. (1997)
4	1,7-Bis(3,4-dimethoxy phenyl)-1,6-heptadiene-3,5-dione	PR	38.3	335360	$C_{23}H_{24}O_6$	396.2 M-H	105; 107; 119; 129; 137; 145; 155; 195	Diarylheptanoid	*Curcuma longa* L.	Chen et al. (2006)
5	(6S)-2-Methyl-6-[(1R,5S)-(4-methene-5-hydroxyl-2-cyclohexen)-2-hepten-4-one	PR	40.2	229164	$C_{15}H_{24}O_2$	236.1 M-H	105; 106; 107; 108; 109; 119; 120; 121; 133; 135	Bisabolane	*Curcuma longa* L.	Li et al. (2011)
6	1,7-Bis(4-hydroxyphenyl)-3,5-heptanediol	KAr	22.8	8120	$C_{19}H_{24}O_4$	316.1 M-H	105; 106; 107; 119; 121; 147; 148	Diarylheptanoid	*Curcuma longa* L.	Ma and Gang (2006)
7	1,7-Bis(3,5-diethyl-4-hydroxyphenyl)-1,6-heptadiene-3,5-dione	KAr	60.6	129145	$C_{27}H_{32}O_4$	420.3 M-H	106; 107; 119; 120; 121; 122; 123; 144; 145; 146; 147; 171; 172; 175; 187; 197; 201; 209; 211; 213; 223; 237; 239; 321; 323	Aromatic	*Curcuma longa* L.	Li et al. (2011)
8	1-(4-Hydroxy-3-methoxyphenyl)-5-(4-hydroxyphenyl)-1,4-pentadiene-3-one	KAv	28.8	8009	$C_{18}H_{16}O_4$	296.1 M-H	105; 109; 117; 119; 133; 145; 159; 161; 171; 173; 181; 185; 1207; 209; 223; 233; 239; 251; 279	Diarylheptanoid	*Curcuma longa* L.	Park and Kim (2002)
9	(-)-(12E,2S,3S,4R, 5R,6R, 9S,11S, 15R)-3,15-Dibenzoyloxy-5,6-epoxylathyr-12-en-14-one	KAv	39.8	5683	$C_{34}H_{38}O_6$	542.2 M-H	119; 145; 183; 211; 212; 237	Diterpenoid	*Euphorbia micractina* Boiss	Tian et al. (2011)
10	5'-methoxycurcumin	PR	35.56	388655	$C_{22}H_{22}O_7$	398.1 M-H	117; 119; 129; 137; 145; 149; 161; 175; 207	Diarylheptanoid	*Curcuma longa* L.	Ravindran (2000)
11	Methyl-7-methoxycoumarin,4-	SU	34.4	67927	$C_{11}H_{10}O_3$	190.1953	115; 116; 117; 119; 120	Coumarin	none	NIST CAS register No. 2555–28–4 Mass Bank ACCESSION: PR100013
12	Hydroferulic acid	KAr	16.8	13992	$C_{10}H_{12}O_6$	195.10 M-H	109; 121; 122	Phenolic acid	*Curcuma longa* L.	Ma and Gang (2006)
13	1,2,3,4-Tetraphenylbutane-2,3-diol	KAr	11.1	3926	$C_{28}H_{26}O_2$	394.1 M-H	112; 129; 133; 180; 207; 243; 247; 263; 339	Aliphatic diol	none	Pubchem Compound ID: 344369
14	4-Hepten-3-one, 5-hydroxy-1,7-bis(4-hydroxyphenyl)-	PR	25.2	1418	$C_{19}H_{20}O_4$	312.1 M-H	118; 119; 120; 146; 161	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
15	5,7-Dihydroxy-2-(4-hydroxyphenyl)-chroman-4-one	PR	26.8	12833	$C_{15}H_{12}O_5$	272.0 M-H	107; 119; 120	Phenolic acids	none	Chromadex
16	Tetradecanoic acid/myristic acid	AS	29.47	2381	$C_{14}H_{28}O_2$	228.0 M-H	128; 130; 143; 155; 158; 182; 183; 184; 210	Fatty acid	none	NIST CAS 544–63–8
17	1-(4-Hydroxy-3-methoxyphenyl)-7-(4-hydroxy-3,5-dimethoxypheny)-4,6-heptadiene-3-one	PR	32.0	194388	$C_{22}H_{24}O_6$	384.1 M-H and M + H	150; 151; 158; 165	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
18	Tumerone	AS	35.3	6120	$C_{15}H_{22}O$	218.0 M-H		Bisabolane sesquiterpene	*Curcuma longa* L.	He (2000)

TABLE 6 | (*Continued*) Cultivar-specific compounds identified by LC-MS in the rhizome extracts from one of the seven cultivars of *Curcuma longa* L. and *C. aromatica* Salisb. The structure of the compound with the serial number "1" is given in Figure 2 (panel number: 36) and compounds with Sl. Nos. 2, 3–9 are given in Figure 4 with the corresponding panel nos. 3, 5–11, respectively. Abbreviations used: AS, Alleppey Supreme; DR, Duggirala Red; PR, Prathibha; SA, Salem; SU, Suguna; KAr, Kasturi Araku; KAv, Kasturi Avidi.

Sl. No.	Compound name	Cultivar	RT (Min)	Area/ abundance	Formula	Mass (m/z)	Mass fragment ions	Class of compound	Reported from plant species	References
19	4-Methylene-5-hydroxybisabola-2,10-diene-9-one	PR	44.6	321246	$C_{15}H_{22}O_2$	234.1 M + H	101; 103; 117; 129; 130; 131; 132; 133; 134; 145; 157; 146; 157; 158; 173; 201	Sesquiterpene	*Curcuma heyneana* Valeton & Zijp	Sirat and Meng (2009)
20	1,7-Bis(3,4-dimethoxyphenyl)-4,4-dimethyl-1,6-heptadiene-3,5-dione	PR	54.4	9854	$C_{25}H_{28}O_6$	447.2 M−H	105; 107; 115; 117; 119; 121; 122; 129; 135 286; 298; 316; 317	Diarylheptanoid	*Curcuma longa* L.	Liang et al. (2009)
21	25-Benzylpentacyclo-(22.3.1.0.)-octacosa-1(27),3 (8),4,6,10(15),11,13,17(22), 18,20, 24(28), 25-dodecaen	AS	54.96	42646	$C_{35}H_{30}$	450.2 M + H	105; 107; 119; 121; 122	Cyclic diarylheptanoid	*Myrica rubra* (Lour.) Siebold & Zucc	Ishida et al. (2002)
22	Palmitic acid	SA	59.5	16809	$C_{16}H_{32}O_2$	256.2 M−H	120; 166	Fatty acid	*Curcuma kwangsiensis* S.K. Lee & C.F. Liang	Jiang et al. (1989)
23	Stearic acid	SA	63.8	76620	$C_{18}H_{36}O_2$	284.1 M−H	197; 199; 200	Fatty acid	*Curcuma longa* L.	Ma and Gang (2006)

Curcuma. Out of the total of 62 compounds detected by LC-MS analyses of rhizome extracts, four compounds were reported for the first time from the *Curcuma* genus. One was cultivar-specific (**Table 6**; Sl. Nos. 1; **Figure 2**, panels: 36), and three were present in more than one cultivar (**Table 7**; Sl. Nos. 1–3). The structures of these first-time reported compounds are given in **Figure 2** (panels: 37–39), and their corresponding mass fragmentation spectra are shown in **Supplementary Figure S2** (panels: 36–39).

A comprehensive table each for GCMS (**Supplementary Table S3**) and LCMS (**Supplementary Table S4**) shows the details of compound identification methods used in the present study for the first-time reported compounds from genus *Curcuma* and the previous literature. A list of 80 (GC-MS) and 62 (LC-MS) compounds can be seen in **Supplementary Tables S5, S6** respectively.

DISCUSSION

In one of our previous studies, we reported that the HPLC method could be a valuable tool to differentiate the cultivars of *Curcuma* spp. based on their curcuminoids content ratios (Kulyal et al., 2016). Curcuminoids play a significant role in food, cosmetics, and medicinal compounds. But there are several other secondary metabolites such as terpenoids (e.g., mono-, sesqui-, di-, tri-, so on), alkenes, aromatic compounds, flavonoids, coumarins, etc. that are responsible for various biological activities. All these secondary metabolites are present in either the volatile essential oil or the nonvolatile fraction of the *Curcuma* spp. Employing untargeted metabolomics would be the ideal way to identify as many metabolites as possible. Therefore, in the present study, we analyzed these secondary compounds using GC-MS and LC-MS/MS.

Versatility of GC-MS and LC-MS Techniques to Identify a Large Number of Metabolites

GC-MS analysis is an appropriate technique for analyzing volatile compounds, whereas LC-MS is for detecting polar compounds, and thus, these two techniques are mutually complementary to each other. In the present study, several of the volatile compounds present in the cultivars of *C. longa* L. and *C. aromatica* Salisb. belonging to mono- and sesquiterpenoids were detected by GC-MS (**Tables 2–4**). On the other hand, LC-MS analysis detected phenolic (**Tables 6–8**) compounds, including several diarylheptanoids in the methanolic extracts of both *C. longa* L. and *C. aromatica* Salisb. (**Figure 4**). Electrospray ionization (ESI), coupled with LC/MS/MS, turned out to be a powerful tool in metabolite profiling and metabolomics research. Studies on chemical derivatization and quantification of several metabolites in turmeric powders and fresh rhizome extracts by LC-MS or LC-MS/MS were made. But the rapid screening within the cultivars of *C. longa* L. of fresh turmeric rhizome has not yet been reported. To the best of our knowledge, we were able to record the presence of several metabolites, which were not reported so far in the *C. longa* L. and *C. aromatica* Salisb. (**Tables 2**, **3**, **6**, **7**, and **Figure 2**), using the available literature search, Metlin library, mass bank, and NIST library.

TABLE 7 | Compounds identified by LC-MS in rhizome extracts of more than one cultivar of *Curcuma longa* L. and *C. aromatica* Salisb. The compounds from serial numbers 1–3 are reported first time from the genus *Curcuma*, the structures of these compounds along with few others are given in **Figure 2** (panels: 37–39; panels 1–2, 4, 12 corresponding to serial numbers 4–5, 6, 7). Abbreviations used: AS, Alleppey Supreme; DR, Duggirala Red; PR, Prathibha; SA, Salem; SU, Suguna; KAr, Kasturi Araku; KAv, Kasturi Avidi.

Sl. No.	Compound name	Cultivar	RT (Min)	Area/ abundance	Formula	Mass (m/z)	Mass fragment ions	Class of compound	Reported from plant species	References
1	5,7,8-Trihydroxy-2′,5′-dimethoxy-3′,4′-methylene dioxyisoflavanone	AS, DR, KAv	2.2	51978	$C_{18}H_{18}O_9$	377.1059 M-H$^-$	101; 102; 113; 119; 161; 163; 228; 336	Flavonoid	*Terminalia ivorensis* A. Chev	Ogundare and Olajuyigbe (2012)
2	Chavicol	AS, SU	38.83	55821	$C_9H_{20}O$	135.0794 M + H$^+$	102; 115 116	Terpenoid	*Piper betle* L.	NIST CAS No: 501–92–8 Nagori et al. (2011)
3	Kaempferol-3-O-rutinoside-7-O-glucoside	PR, SA	33.2	3752	$C_{33}H_{40}O_{20}$	755.2655 M- H$^-$	135; 161; 175; 176; 191; 439; 579; 755; 756	Flavonoid	*Lycopersicon esculentum* Mill	Le Gall et al. (2003)
4	Kaempferol-3-rhamnoside	AS, DR	10.76	5367	$C_{21}H_{20}O_{10}$	431.9911 M-H	125; 142; 146; 150 176; 184 190; 293; 304; 308 311; 316; 343; 345	Flavonoid	*Curcuma Xanthorrhiza* Roxb	Ruslay et al. (2007)
5	3-Acetyl coumarin	AS, PR, SA, SU, KAv	34.65	289624	$C_{11}H_8O_3$	188.0534	115; 116; 117; 118 141; 143	Coumarin	None	Pub Chem ID 24852845 NIST 3949–36–8
6	Turmeronol	AS, DR, SU	25.36	87260	$C_{15}H_{20}O_2$	232.1436	103; 104; 105 107; 115; 117; 118 119; 120; 121; 128 129; 131; 141; 142; 143	Bisabolane sesquiterpene	*Curcuma longa* L.	Ma and Gang (2006)
7	7-(3,4-Dihydroxyphenyl)-5-hydroxy-1-phenyl-(1E)-1-heptene	AS, KAv	35.99	16570	$C_{19}H_{22}O_3$	298.1 M-H	119; 183; 184	Diarylheptanoid	*Curcuma xanthorrhiza* Roxb	Suksamrarn et al. (1994)
8	1,7-Diphenyl-1,6-heptadiene-3,5-dione	AS, SA	2.49	9697	$C_{19}H_{16}O_2$	276.0	115	Diarylheptanoid	Synthesized the compound	Sundaryono et al. (2003)
9	1-Hepten-3-one, 5-hydroxy-1,7-bis(3,4-dihydroxyphenyl)-	PR, SA, SU, KAr, KAv	21.2	1660	$C_{19}H_{20}O_6$	344.1	107; 121; 134; 135; 136; 159; 161; 162; 177; 178	Diarylheptanoid	*Alnus japonica* (Thunb.) Steud	Sati et al. (2011)
10	4-(*p*-Hydroxyphenyl)-3-buten-2-one	AS, DR, SA, KAv	22.16	18641	$C_{10}H_{10}O_2$	162.0	117; 118	Flavonoid	None	NIST CAS 3160–35–8
11	5-Hydroxy-7-(4-hydroxyphenyl)-1-phenyl-(1E)-1-heptene	AS, DR, PR, SA, KAr, KAv	23.11	6169	$C_{20}H_{24}O_4$	328.1	107; 119; 133; 134; 135; 136; 159; 161; 162; 177; 178	Diarylheptanoid	*Curcuma xanthorrhiza* Roxb	Suksamrarn et al. (1994)
12	1-(4-Hydroxy-3-methoxyphenyl)-7-(4-hydroxy-3,5-dimethoxypheny)-4,6-heptadiene-3-one	AS, DR, SA, KAr, KAv	25.8	6408	$C_{22}H_{24}O_6$	384.1	133; 134; 147; 148; 150; 151; 158; 165; 175; 176; 186; 187; 188; 189; 203; 204; 232	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
13	1,5-Bis(3,4-methylenedioxyphenyl)-1,4-pentadien-3-one	SU, KAv	26.0	9161	$C_{19}H_{14}O_5$	322.0	115; 119; 121; 133; 143; 235; 237; 247; 263; 275	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
14	1-Hydroxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-6-hepten-3,5-dione	AS, KAv	26.7	45589	$C_{20}H_{20}O_7$	372.1	103; 117; 131; 137; 143; 145; 149; 163; 177	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
15	1,7-Bis(4-hydroxyphenyl)-1-heptene-3,5-dione	AS, DR, PR, SA, SU, KAv	27.4	8495	$C_{19}H_{18}O_4$	310.1	117; 118; 119; 145; 146; 161; 175; 176	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
16	1,7-Bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one	AS, DR, PR, SA, SU, KAv	30.0	7240	$C_{19}H_{16}O_3$	292.1	115; 117; 119; 120; 143; 145	Diarylheptanoid	*Curcuma longa* L.	Li et al. (2011)
17	7-(4-Hydroxy-3-methoxyphenyl)-1-(4-hydroxy phenyl)-4,6-heptadien-3-one	AS, KAv	31.8	138675	$C_{20}H_{20}O_4$	324.1	107; 117; 119; 120; 122; 123; 131; 135; 137; 145; 146; 147; 148; 163; 195; 223	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)

TABLE 7 | (*Continued*) Compounds identified by LC-MS in rhizome extracts of more than one cultivar of *Curcuma longa* L. and *C. aromatica* Salisb. The compounds from serial numbers 1–3 are reported first time from the genus *Curcuma*, the structures of these compounds along with few others are given in Figure 2 (panels: 37–39; panels 1–2, 4, 12 corresponding to serial numbers 4–5, 6, 7). Abbreviations used: AS, Alleppey Supreme; DR, Duggirala Red; PR, Prathibha; SA, Salem; SU, Suguna; KAr, Kasturi Araku; KAv, Kasturi Avidi.

Sl. No.	Compound name	Cultivar	Area/ abundance	RT (Min)	Formula	Mass (m/z)	Mass fragment ions	Class of compound	Reported from plant species	References
18	Coumaran	AS, DR, SA, SU	6563	34.36	C_8H_8O	120.0	116; 117; 118; 119	Coumarin	None	Chromadex
19	5,7-Dihydroxy-4-methylcoumarin	AS, SA, SU, KAv	92188	34.57	$C_{10}H_8O_4$	192.17	113; 115; 116; 117; 118; 141	Coumarin	None	PubChem CID 5354284
20	1,7-Bis(3,4,5-trimethoxyphenyl)-1,6-heptadiene-3,5-dione	PR, SU, KAr, KAv	4972	35.82	$C_{25}H_{28}O_8$	456.3	280; 281; 298; 299	Diarylheptanoid	Synthesised the compound	Hahm et al. (2002)
21	Curlone	AS, DR, PR, SU, KAr, KAv	19540	46.50	$C_{15}H_{22}O$	218.0	101; 103; 117; 129; 130; 131; 132; 133; 134; 145; 157; 146; 157; 158; 173	Bisabolane sesquiterpene	*Curcuma longa* L.	He (2000)
22	Hydrocinnamic acid	SU, KAr	3812	35.1	$C_9H_{10}O_2$	150.0	103; 105; 133	Phenolic acid	*Curcuma longa* L.	Ma and Gang (2006)
23	Curcumenol	AS, SU, KAr, KAv	34556	36.67	$C_{15}H_{22}O_2$	234.1	105; 107; 109; 117; 123; 125; 133; 137	Sesquiterpene	*Curcuma heyneana* Valeton & Zijp	Sirat and Meng (2009)
24	Oleic acid	SA, KAr	15974	60.2	$C_{18}H_{34}O_2$	282.1	168; 257	Fatty acid	*Curcuma longa* L.	Ma and Gang (2006)

Cultivar Variability Based on Secondary Metabolites

Based on the presence or absence of metabolites identified by GC-MS and LC-MS analyses, there was a need to authenticate cultivar variability. Thus, the metabolite library can be constructed based on the cultivar-specific and compounds found in more than one cultivar. There are very few reports on cultivar-specific secondary metabolite variation. Out of a total of 142 compounds identified by both GC-MS and LC-MS, only 28 compounds (13 from GCMS and 15 from LCMS) were common (**Tables 4**, **8**) present in all the cultivars of *C. longa* L. and *C. aromatica* Salisb. Ten of 13 common compounds (GCMS) were reported earlier from *C. longa* L. rhizome. Two compounds, namely sabinene and α-caryophyllene, were reported from the leaves of *C. longa* L. The remaining one compound, i.e., 2-heptadecanone, was detected for the first time from these two Curcuma species. This compound was earlier reported in the essential oil of *Curcuma angustifolia* Roxb. rhizome (Srivastava et al., 2006).

As per our analyses, 64 compounds (**Tables 2**, **6**) out of 142 compounds were cultivar-specific. Of these 64 compounds, 41 were identified in essential oils by GC-MS (e.g., carvacrol, endo-borneol) and 23 (e.g., tumerone, methyl-7-methoxycoumarin,4-) in fresh rhizome extracts (LC-MS) of any one of the cultivars of *C. longa* L. or *C. aromatica* Salisb. In addition, 50 compounds (**Tables 3**, **7**) were identified to be present in some of the cultivars, present in more than one cultivar but not common to all the cultivars of *C. longa* L. and *C. aromatica* Salisb. Out of these 50 compounds, 26 were identified in essential oils through GC-MS. For example, 1,3,5-cycloheptatriene was detected in all six cultivars except cv. Duggirala Red, whereas 12-oxabicyclo(9.1.0)dodeca-3,7-diene, 1,5,5,8-tetramethyl-, [1R-(1R*,3E,7E,11R*)]-, was detected only in cvs. Duggirala Red and Kasturi Araku. The rest 24 compounds were detected in rhizome extracts by LC-MS (e.g., chavicol detected in cvs. Alleppey Supreme and Suguna). The present extensive analyses of both essential oils and whole rhizome secondary metabolome of seven cultivars of *C. longa* L. and *C. aromatica* Salisb. established cultivar variability. Variability of the compounds within or/and in between the cultivars of *C. longa* L. and *C. aromatica* Salisb. will give a better understanding of their selection. The current study will help select cultivars for use in pharmacology or the food industry.

Discovery of First-Time Reported Metabolites in *C. longa* L. and *C. aromatica* Salisb.

In the present study, as many as 142 compounds were identified in the essential oils and rhizome extracts of *C. longa* L. and *C. aromatica* Salisb. Out of these, 39 compounds were identified for the first time in the genus *Curcuma*. However, these compounds were found in other plant genera. The structures of these compounds are shown in **Figure 2**, and corresponding details, including the class of compound, molecular weight, are given in **Tables 2**, **3**, **6**, and **7**. As an example, cv. Alleppey Supreme of *C. longa* L. showed three cultivar-specific compounds. Among these, 1,2-cyclohexanediol, 1-methyl-4-(1-methylethyl)- (oxygenated

TABLE 8 | Compounds commonly detected by LC-MS analysis of rhizomes extract of all seven cultivars of *Curcuma* spp.: five of *Curcuma longa* L. (cvs. Alleppey Supreme, Duggirala Red, Prathibha, Salem, and Suguna) and two of *C. aromatica* Salisb. (cvs. Kasturi Araku, Kasturi Avidi). The structures for the compounds in the serial numbers 10, 5, 6, 15, and 1 are given in **Figure 4** (panels 13, 14, 15, 16, and 17 respectively).

Sl. No.	Compound name	RT (Min)	Area/ abundance	Formula	Mass (m/z)	Mass fragment ions	Class of compound	Reported from plant species	References
1	1,5-Bis(4-hydroxy-3-methoxyphenyl)-1,4-pentadien-3-one	23.5	3535	$C_{19}H_{18}O_5$	325.1247	117; 118; 119; 120 135; 143; 145; 146 159; 161; 187	Diarylheptanoid	*Curcuma longa* L.	Li et al. (2011)
2	Ar-Turmerone	24.7	23545	$C_{15}H_{20}O$	216.1	103; 104; 105; 106; 107; 108; 115; 116; 117; 118; 119; 120	Bisabolane sesquiterpene	*Curcuma longa* L.	Parthasarathy and Chempakam (2008)
3	Tetrahydroxybisdemethoxycurcumin	25.4	4773	$C_{19}H_{20}O_4$	311.1446	117; 118; 119; 120 146; 161	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
4	Tetrahydrodemethoxycurcumin	25.9	7734	$C_{20}H_{22}O_5$	341.1272	101; 113; 119	Diarylheptanoid	*Piper nigrum* L.	Ravindran (2000)
5	1-(4-Hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-1,4,6-heptatrien-3-one	26.1	76458	$C_{20}H_{18}O_4$	321.0938	115; 117; 119; 121 132; 133; 134; 143 145; 174; 235; 237 247; 263'264; 274 275	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
6	1,7-Bis(4-hydroxy-3-methoxyphenyl)-1,4,6-heptatrien-3-one	26.3	64172	$C_{21}H_{20}O_5$	351.1123	108; 115; 119; 136 143; 148; 164; 195 207; 223; 224; 235 245; 251; 261; 262 263; 279; 291; 307	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
7	Tetrahydroxycurcumin	26.5	81260	$C_{20}H_{20}O_7$	371.1686	133; 134; 135; 148 149; 175; 176; 177	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
8	1-(4-Hydroxy-3-methoxyphenyl)-7-(4-hydroxy-3,5-dimethoxyphenyl)-1,4,6-heptatrien-3-one	26.84	58571	$C_{22}H_{22}O_6$	382.1	149; 159; 173; 197; 209; 211; 221; 233; 237; 239; 249; 261; 267; 277; 289; 293; 295; 305; 309	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
9	1,6-Heptadiene-3,5-dione, 1-(3,4-dihydroxyphenyl)-7-(4-hydroxy phenyl)-	31.6	5753	$C_{19}H_{16}O_5$	324.1	134; 135; 136; 143	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
10	1-(3,4-Dihydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-hepta-1,6-diene-3,5-dione	32.3	16375	$C_{20}H_{18}O_6$	353.1212	134; 135; 136; 150	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
11	Bisdemthoxycurcumin	34.5	1675644	$C_{19}H_{16}O_4$	307.1132	117; 119; 120; 143 145	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
12	Demethoxycurcumin	35.4	1302410	$C_{20}H_{18}O_5$	337.1251	117; 119; 120; 132 134; 143; 145; 158 160; 175; 201	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
13	Dihydrocurcumin	35.8	5151	$C_{21}H_{22}O_6$	369.1533	132; 134; 135; 149	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)

(Continued on following page)

TABLE 8 | (*Continued*) Compounds commonly detected by LC-MS analysis of rhizomes extract of all seven cultivars of *Curcuma* spp.: five of *Curcuma longa* L. (cvs. Alleppey Supreme, Duggirala Red, Prathibha, Salem, and Suguna) and two of *C. aromatica* Salisb. (cvs. Kasturi Araku, Kasturi Avidi). The structures for the compounds in the serial numbers 10, 5, 6, 15, and 1 are given in Figure 4 (panels 13, 14, 15, 16, and 17 respectively).

Sl. No.	Compound name	RT (Min)	Area/ abundance	Formula	Mass (m/z)	Mass fragment ions	Class of compound	Reported from plant species	References
14	Curcumin	36.2	1503497	$C_{21}H_{20}O_6$	367.1374	158; 160; 175 132; 133; 134; 135 149; 158; 160; 161 175	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)
15	1-Heptene-3,5-dione, 1,7-bis-(4-hydroxy-3-methoxyphenyl)-	43.2	5078	$C_{20}H_{20}O_5$	339.1473	117; 119; 120; 134 158	Diarylheptanoid	*Curcuma longa* L.	Jiang et al. (2006)

alcoholic monoterpenoid) was earlier reported from leaf and peel essential oil of *Citrus medica* L. (Rutaceae). This compound is used as a flavoring agent (Bhuiyan et al., 2009); trans, trans-octa-2,4-dienyl acetate, present in common Malaysian *Kaempferia galanga* L. (Zingiberaceae), was used for its food-flavoring property (Othman et al., 2006). Phenol, 2-methoxy-3-(2-propenyl)-, an allyl chain-substituted guaiacol was reported from rosewood extracts (Jiang et al., 2018).

The following four compounds were identified from cv. Duggirala Red (*C. longa* L.): 3-isopropyl-4-methyl-1-pentyn-3-ol (alcohol constituent) containing leaf and stem of *Anethum sowa* Roxb. ex, Fleming, used for flavoring of food, beverages and also for many medical preparations (Saleh-e-in et al., 2010); 5,9-tetradecadiyne (unsaturated hydrocarbon) was found to be a major component of *Ferula vesceritensis* Coss. & Durieu ex Trab. leaf essential oil (Zellagui et al., 2012); naphthalene, 5-butyl-1,2,3,4-tetrahydro- (tetralin type of compounds) found in the essential oil of *Meconopsis punicea* Maxim. and *M.delavayi* (Franch.) Franch. Ex Prain (Slavík and Slavíková; Yuan et al., 2003); and santolina alcohol was reported from plant *Achillea filipendulina* Lam. (Sharopov and Setzer, 2010). A total of nine cultivar-specific compounds were detected in cv. Prathibha (*C. longa* L.) and the examples of these compounds and their source plants, respectively, are 7-tetracyclo[6.2.1.0(3.8)0(3.9)]undecanol, 4,4,11,11 tetramethyl- in *Cyperus articulatus* L. (Metuge et al., 2014); bicyclo(2.2.1)hept-2-ene, 2,3-dimethyl- in *Abies alba* Mill. (Yang et al., 2009). Cultivar-specific compounds of three each were detected in cvs. Salem (*C. longa* L.) and Suguna (*C. longa* L.) (**Table 2**). In *C. aromatica* Salisb., only one cultivar-specific compound was detected in cv. Kasturi Avidi, i.e., 3-octen-5-yne, 2,7-dimethyl-, (Z)-, and this compound was earlier reported from the medicinally important *Litsea glutinosa* (Lour.) C.B. Rob. fruit essential oil (Chowdhury et al., 2008a).

Some of the compounds identified in our study were present in more than one cultivar. For example, 6-(p-tolyl)-2-methyl-2-heptenol (**Table 3**) was detected in three cvs.: Alleppey supreme, Suguna of *C. longa* L., and Kasturi Avidi of *C. aromatica* Salisb. This compound was earlier reported from *Zingiber officinale* Roscoe (Zingiberaceae), used as a spice, food products, and beverages (Choudhari and Kareppa, 2013).

Limitations and Strengths of the Present Study

There is significant variability within and between the cultivars of *C. longa* L. and *C. aromatica* Salisb, which can be exploited to differentiate the cultivars of *Curcuma* spp. The feasibility of studies without using any standard compounds was pointed out by Núñez et al. (2020). Similarly, reference compounds were not used in our study to derive arithmetic indices under the experimental conditions. Despite the dilution made in the essential oil sample before injecting into the GC-MS system, the sample was still too concentrated. The high concentration of oil might have restricted the resolution due to overloading the detector. This could be the reason that we could not identify several compounds. We would ensure the further dilution of the oil sample in our future studies. However, the technology employed, GC-TOFMS and LC-QTOFMS, and MS-spectral database/literature search enabled us to establish the cultivar variability of *Curcuma* spp. The detailed information on the metabolite variability within or/and between the cultivars of *C. longa* L. and *C. aromatica* Salisb. may assist us in selecting the cultivars for a specific purpose, like culinary use, coloring, or pharmacological purpose. The studies such as the present one can help to select cultivars, particularly for use in pharmacology or the food industry. Metabolite variability poses a challenge in the use of turmeric in therapy. The practitioners need to be quite careful and use the identified cultivar and avoid mix-up. The caution applies to commercial/industrial use. Once standardized, the protocol should ensure the use of a specific cultivar. Our GC-MS and LC-MS-based metabolite identification is distinct from chemophenetic studies but is a complementary approach to characterize the *Curcuma* metabolome.

Importance of *Curcuma* spp. Metabolites for Human Health

Curcuminoids (CU, DMC, and BDMC) were identified as the main bioactive compounds of genus *Curcuma* and proved to have a broad spectrum of biological activities based on pharmacological studies. However, rhizomes and their essential oils of *Curcuma* spp. contained several other

TABLE 9 | Pharmacological activity of metabolites identified, other than major curcuminoids (curcumin, demethoxycurcumin, and bisdemethoxy curcumin), in *C. longa* L. and *C. aromatica* Salisb.

Sl. No.	Compound name	Source plant	Tested Compound/ essential oil/extract	Pharmacological activity/health benefit of the compound or compound containing plant product	References (Activity assay or compound detection)
1	Carvacrol	*Curcuma longa* L.	Compound	Antibacterial	Suntres et al. (2015)
2	p-Cymene	*Curcuma longa* L.	Compound	Antioxidant	(De Oliveira et al. (2015)
				Anti-inflammatory, anticancer, and antimicrobial effects	Marchese et al. (2017)
3	Eucalyptol	*Curcuma longa* L.	Compound	Antitumor anti-inflammatory relevance to Alzheimer's disease	Murata et al. (2013); Islam et al. (2014)
4	α-Pinene	*Curcuma longa* L.	Compound	Anti-inflammatory and chondroprotective	Rufino et al. (2014)
5	α-Terpineol	*Curcuma longa* L.	Compound	Anti-inflammatory	De Oliveira et al. (2012)
6	Terpinolene	*Curcuma longa* L.	Compound	Anticancer	Okumura et al. (2012)
7	2-Heptadecanone	*Curcuma angustifolia* Roxb	Dried rhizome essential oil	As a coolant, demulscent	Srivastava et al. (2006)
8	Santolina alcohol	*Achillea filipendulina* Lam	Aerial part essential oil	Traditional herbal medicine	Sharopov and Setzer (2010)
9	Cyclohexanol, 2-methyl-5-(1-methylethenyl)-	*Mentha spicata* L.	Aerial parts essential oil	Antifungal	Mohammed et al. (2017)
10	Cyclohexane, 1,2-dimethyl-3,5-bis(1-methylethenyl)-	*Rhanterium adpressum* Coss. & Durieu	Aerial parts essential oil	Antifungal	Kala et al. (2009)
11	4-Ethylphenethylamine	*Psidium guajava* L.	Stem bark essential oil	Antioxidant	Fasola et al., 2011)
12	5,9-Tetradecadiyne	*Ferula vesceritensis* Coss. & Durieu ex Trab	Leaves essential oil	Antibacterial	Zellagui et al. (2012)
13	E-11-Tetradecenoic acid	*Coriandrum sativum* L.	Leaf essential oil	Spice, flavoring agent, antimicrobial	Bhuiyan et al. (2009)
14	6,10-Dodecadien-1-yn-3-ol, 3,7,11-trimethyl-	*Hiptage benghalensis* (L.) Kurz	Leaves essential oil	Treatment of skin diseases, cough, asthma, leprosy	Venkataramani and Chinnagounder (2012)
15	Chavicol	*Piper betle* L.	Leaf oil	Antifungal, antiseptic, and anthelmintic	Nagori et al. (2011)
16	1,2-Cyclohexanediol, 1-methyl-4-(1-methylethyl)-	*Citrus medica* L.	Leaf and peel essential oil	Antibiotic	Bhuiyan et al. (2009)
17	3-Isopropyl-4-methyl-1-pentyn-3-ol	*Anethum sowa* Roxb. ex, Fleming	Leaf and stem essential oil	Flavoring of food and beverages, antimicrobial, antioxidant	Saleh-e-in et al. (2010)
18	Bicyclo(2.2.1)hept-2-ene, 2,3-dimethyl-	*Abies alba* Mill	Leaf and twig essential oil	Radical scavenging activity	Yang et al. (2009)
19	2-Nonen-4-yn-1-ol, (Z)-	*Alpinia speciosa* (J.C. Wendl.) K. Schum	Seeds and leaves essential oil	As a food and herbal medicine, mosquito larvicidal activity	Ho (2010)
20	8-Methylene-3-oxatricyclo [5.2.0.0(2,4)]nonane	*Schisandra chinensis* (Turcz.) Baill	Dried fruit essential oil	Antioxidant	Wang et al. (2005)
21	3-Cyclohexen-1-one, 3,5,5-trimethyl-	*Crocus sativus* L.	Dried saffron oil	Antitumor	(D'Auria et al. (200
22	Ar-Tumerone α-Turmerone β-Turmerone α-Santalene Ar-Curcumene	*Curcuma longa* L.	Rhizome essential oil	Antioxidant	Singh et al. (2010)
23	7-Tetracyclo[6.2.1.0(3.8)0(3.9)] undecanol, 4,4,11,11 tetramethyl-	*Cyperus articulatus* L.	Roots/rhizome essential oil	Anti-onchocera activity	Metuge et al. (2014)
24	Cholesta-8,24-dien-3-ol, 4-methyl-, (3á,4à)-	*Parkia speciosa* Hassk.	Seed essential oil	High nutritional and medicinal value	Salman et al. (2006)
25	3-Octen-5-yne, 2,7-dimethyl-, (Z)-	*Litsea glutinosa* (Lour.) C.B. Rob	Fruit essential oil	Antirheumatic	Chowdhury et al. (2008b)
26	5,8,11,14-Eicosatetraenoic acid, phenylmethyl ester, (all-Z)-	*Petiveria alliacea* L.	Whole plant essential oil	Used as folk medicine to enhance memory and in treatment of common cold, flu, other viral, or bacterial infections	Sathiyabalan et al. (2014)
27	Naphthalene, 5-butyl-1,2,3,4-tetrahydro-	*Meconopsis punicea* Maxim. and *M. delavayi* (Franch.) Franch. Ex Prain	Whole plant essential oil	As a traditional medicinal plant for anti-inflammatory and analgesic activity	Yuan et al. (2003)
28	1H-3a,7-methanoazulene, 2,3,4,7,8,8a-hexahydro-3,6,8,8-tetramethyl-, [3R-(3à,3aá,7á,8aà)]-	*Lindera aggregata* (Sims) Kosterm	Root/tubers essential oil	Treatment of decubitus ulcer	Hong (2011)
29	trans, trans-Octa-2,4-dienyl acetate	*Kaempferia galanga* L.	Dried rhizomes	Spice, food-flavoring agent	Othman et al. (2006)

(Continued on following page)

TABLE 9 | (*Continued*) Pharmacological activity of metabolites identified, other than major curcuminoids (curcumin, demethoxycurcumin, and bisdemethoxy curcumin), in *C. longa* L. and *C. aromatica* Salisb.

SI. No.	Compound name	Source plant	Tested Compound/ essential oil/extract	Pharmacological activity/health benefit of the compound or compound containing plant product	References (Activity assay or compound detection)
30	11-Dodecen-2-one	*Ficus hispida* L. f	Fresh male and female receptive figs	Vasorelaxant Hepatoprotective, anti-inflammatory, antipyretic	Song et al. (2001)
31	Kaempferol-3,7-O-dimethyl ether	*Lumnitzera racemosa* Willd and *Artemisia vulgaris* L.	Fresh twig methanolic extract; leaf methanolic extract	Antibacterial	Nikolova (2006); DeSouza et al. (2010)
32	5,7,8-Trihydroxy-2′,5′-dimethoxy-3′,4′-methylene dioxyisoflavanone	*Terminalia ivorensis* A. Chev	Fresh sawdust methanolic extract	Antifungal	Ogundare and Olajuyigbe (2012)
33	Kaempferol-3-O-rutinoside-7-O-glucoside	*Lycopersicon esculentum* Mill	Methanolic extract of fruit	Antioxidant	Le Gall et al. (2002)
34	Phenol, 2-methoxy-3-(2- propenyl)-	*Dalberga stevensonii* Standl	Wood extracts	Used as raw material for medical industries	Jiang et al. (2018)
35	2-Pentanone, 4-mercapto-4-methyl-	*Camellia sinensis* (L.) Kuntze	Tea leaves	Antioxidant	Kumazawa et al. (2005)

bioactive (volatile and nonvolatile) compounds. A summary of the pharmacological studies with the metabolites detected in the present study is given in **Table 9**. Some of the studies demonstrated therapeutic activity with the isolated metabolites, e.g., carvacrol (Suntres et al., 2015), p-cymene (De Oliveira et al., 2015), which are commonly found in essential oils of *Curcuma* spp. A few other reports correlated anti-inflammatory and antioxidant properties of *C. longa* L. essential oil with its chemical components ar-tumerone, α-santalene (Singh et al., 2010) (**Table 9**). Several compounds detected in the present study in the essential oil or rhizome extracts of *C. longa* L. or *C. aromatica* Salisb. were also found in the essential oil of other medicinal plants, traditionally used for their health benefits. The examples of such compounds are 5,9-tetradecadiyne, a cultivar-specific compound of Duggirala Red (*C. longa* L.), earlier reported in *Ferula vesceritensis* Coss. & Durieu ex Trab. leaf essential oil, exhibiting antibacterial activity; 3-octen-5-yne, 2,7-dimethyl-, (Z)-, a hydrocarbon monoterpene, identified from cv. Kasturi Avidi (*C. aromatica* Salisb.) was earlier reported from fruit essential oil of the medicinally important plant, *Litsea glutinosa* (Lour.) C.B. Rob. (Chowdhury et al., 2008a). We suggest that the medicinal use of the genus *Curcuma* can be not only species but also cultivar-specific.

CONCLUDING REMARKS

Essential oils from spices and aromatic plants are enriched with bioactive metabolites, easily isolated and used, unlike the difficulties encountered with synthetic chemical products. The low mammalian toxicity and biodegradable nature of the natural secondary products provide an attractive option to develop them also for crop protection. Metabolomics is a practical and dynamic approach to make a comprehensive

study. Both GC-MS and LC-MS techniques should be used to characterize the metabolite profiles of as many cultivars as possible for building a reference library. Preparative LC can be helpful to collect individual metabolite fractions and establish their identity. Several metabolites detected in 7 selected cultivars of *Curcuma* spp. by GC-MS and LC-MS analyses are reported first time in *Curcuma* spp. We suggest that the seven Indian cultivars of *Curcuma* spp. employed in our study can be used as sources of such compounds. High-throughput analysis of cultivar-specific and first-time detected compounds in the present study may lead to new drug candidates. The metabolites validated for their medicinal or other users can be quantified using simple techniques such as HPLC or TLC to ensure their presence in the herbal preparations.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: https://www.ebi.ac.uk/metabolights/MTBLS2790.

AUTHOR CONTRIBUTIONS

ST and AR planned and designed all the experiments. PK and PKK did the experiments and preliminary data interpretation related to GC-MS and LC-MS/MS, respectively. PK, ST, and AR re-analyzed the data and wrote the draft of the manuscript. SA prepared tables and reference search. AA drew the figures and helped in editing the manuscript. All the authors read and approved the final version of the manuscript.

FUNDING

ACKNOWLEDGMENTS

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphar.2021.659546/ full#supplementary-material

Supplementary Figure 1 | **(A)** Representative TIC chromatograms from negative ion (–) ESI-HPLC from cultivars (A) Alleppey Supreme, (B) Duggirala Red, (C) Prathibha, (D) Salem, (E) Suguna of *Curcuma longa* L. and cvs. (F) Kasturi Araku, (G) Kasturi Avidi of *C. aromatica* Salisb. Peak labelled IS represents internal standard. **(B)** Representative TIC chromatograms from positive ion (+) ESI-HPLC from cultivars (A) Alleppey Supreme, (B) Duggirala Red, (C) Prathibha, (D) Salem, (E) Suguna of *Curcuma longa* L. and cvs. (F) Kasturi Araku, (G) Kasturi Avidi of *C. aromatica* Salisb. Peak labelled IS represents internal standard.

Supplementary Figure 2 | MS and MS/MS spectra of cultivar-specific compounds first time reported from genus *Curcuma*, identified from cultivars of *Curcuma longa* L. and *C. aromatica* Salisb. detected in essential oil (1–35) and rhizome extracts (36–39) by GC-MS (MS spectra) and LC-MS (MS/MS spectra) respectively. (Spectra 1–23 corresponds to panel numbers: 1–23 of **Figure 2** and serial numbers: 1–23 of Table 2. Spectra 24–35 corresponds to panel numbers: 24–35 of **Figure 2** and serial numbers: 1–12 of **Table 3**. Spectra 36 correspond to panel numbers 36 of **Figure 2** and serial number 1 of **Table 6**. Spectra 37–39 correspond to panel number 37–39 of **Figure 2** and serial number 1–3 of **Table 7**). (1) 1,2-Cyclohexanediol, 1-methyl-4-(1-methylethyl)-, (2) trans, trans-Octa-2,4-dienyl acetate, (3) Phenol, 2-methoxy-3-(2- propenyl)-, (4) 3-Isopropyl-4-methyl-1-pentyn-3-ol (5) 5,9-Tetradecadiyne, (6) Naphthalene, 5-butyl-1,2,3,4-tetrahydro-, (7) Santolina alcohol, (8) 2-Pentanone, 4-mercapto-4-methyl-, (9) 8-Methylene-3-oxatricyclo[5.2.0.0(2,4)]nonane, (10) 7-Tetracyclo[6.2.1.0(3.8)0(3.9)]undecanol, 4,4,11,11 tetramethyl-, (11) Bicyclo[2.2.1]hept-2-ene, 2,3-dimethyl-, (12) 1H-3a,7-Methanoazulene, 2,3,4,7,8,8a-hexahydro-3,6,8,8-tetramethyl-, [3R-(3à,3aá, 7á, 8aà)]-, (13) Cholesta-8,24-dien-3-ol, 4-methyl-, (3á,4à)-, (14) 4-Ethylphenethylamine, (15) Cyclohexanol, 2-methyl-5-(1-methylethenyl)-, (16) Cyclohexane, 1,2-dimethyl-3,5-bis(1-methylethenyl)-, (17) 5,8,11,14-Eicosatetraenoic acid, phenylmethyl ester, (all-Z)-, (18) 11-Dodecen-2-one, (19) E-11-Tetradecenoic acid, (20) 2-Nonen-4-yn-1-ol, (Z)-, (21) 3-Cyclohexen-1-one, 3,5,5-trimethyl-, (22) 6,10-Dodecadien-1-yn-3-ol, 3,7,11-trimethyl-, (23) 3-Octen-5-yne, 2,7-dimethyl-, (Z)-, (24) 1,3,5-Cycloheptatriene, (25) Bicyclo[3.1.0] hexane, 4-methyl-1-(1-methylethyl)-, didehydro deriv.-, (26) Bicyclo[3.2.1]oct-2-ene, 3-methyl-4-methylene-, (27) Oxirane, 2-(hexyn-1-yl)-3-methoxymethylene-, (28) Bergamotol, Z-α-trans-, (29) (1,3-Dimethyl-2-methylene-cyclopentyl)-methanol, (30) 12-Oxabicyclo[9.1.0]dodeca-3,7-diene, 1,5,5,8-tetramethyl-, [1R-(1R*,3E,7E,11R*)]-, (31) Isolongifolene, 4,5,9,10-dehydro-, (32) Z,Z,Z-4,6,9-Nonadecatriene, (33) 6-(p-Tolyl)-2-methyl-2-heptenol, (34) 6-Tridecen-4-yne, (Z)-, (35) 1,4-Cyclohexadiene, 1-methyl-, (36) Kaempferol-3,7-O-dimethyl ether, (37) 5,7,8-Trihydroxy-2′,5′-dimethoxy-3′,4′-methylene dioxyisoflavanone, (38) Chavicol, (39) Kaempferol-3-O-rutinoside-7-O-glucoside.

Supplementary Table 1 | A list of secondary metabolites identified by GC-MS in the essential oil from the rhizomes of five cvs. of *C. longa* L. and two cvs. of *C. aromatica* Salisb. Abbreviations: AS, Alleppey Supreme; DR, Duggirala Red; PR, Prathibha; SA, Salem; SU, Suguna; KAr, Kasturi Araku; KAv, Kasturi Avidi.

Supplementary Table 2 | A list of secondary metabolites identified by LC-MS in the rhizomes extract of five cvs. of *C. longa* L. and two cvs. of *C. aromatica* Salisb. Abbreviations used: AS, Alleppey Supreme; DR, Duggirala Red; PR, Prathibha; SA, Salem; SU, Suguna; KAr, Kasturi Araku; KAv, Kasturi Avidi.

Supplementary Table 3 | Identification parameters of first-time reported compounds by GC-MS in the essential oil from the seven cultivars of *Curcuma* spp. along with the methods used in previous literature.

Supplementary Table 4 | Identification parameters of first-time reported compounds by LC-MS in the rhizome extracts of genus *Curcuma* along with the methods used in related previous literature.

Supplementary Table 5 | The list of 80 compounds identified by GCMS analysis.

Supplementary Table 6 | The list of 62 compounds identified by LCMS analysis.

REFERENCES

Aggarwal, B. B., Sundaram, C., Malani, N., and Ichikawa, H. (2007). "Curcumin: The Indian Solid Gold,," in *The Molecular Targets and Therapeutic Uses of Curcumin in Health and Disease*. Editors B. B. Aggarwal, Y.-J. Surh, and S. Shishodia (Boston, MA: Springer US), 1–75. doi:10.1007/978-0-387-46401-5_1

Angel, G. R., Menon, N., Vimala, B., and Nambisan, B. (2014). Essential Oil Composition of Eight Starchy *Curcuma Species*. *Ind. Crops Prod.* 60, 233–238. doi:10.1016/j.indcrop.2014.06.028

Awasthi, P. K., and Dixit, S. C. (2009). Chemical Composition ofCurcuma Longaleaves and Rhizome Oil from the plains of Northern India. *J. Young Pharm.* 1, 312. doi:10.4103/0975-1483.59319

Beekwilder, J., Jonker, H., Meesters, P., Hall, R. D., Van Der Meer, I. M., and Ric de Vos, C. H. (2005). Antioxidants in Raspberry: On-Line Analysis Links

Antioxidant Activity to a Diversity of Individual Metabolites. *J. Agric. Food Chem.* 53, 3313–3320. doi:10.1021/jf047880b

Behura, S., Sahoo, S., and Srivastava, V. K. (2002). Major Constituents in Leaf Essential Oils of *Curcuma Longa* L. And *Curcuma Aromatica* Salisb. *Curr. Sci.* 83, 1312–1313.

Bhuiyan, M. N. I., Begum, J., Sardar, P. K., and Rahman, M. S. (2009). Constituents of Peel and Leaf Essential Oils of *Citrus Medica* L. *J. Sci. Res.* 1, 387–392. doi:10.3329/jsr.v1i2.1760

Chen, W. F., Deng, S. L., Zhou, B., Yang, L., and Liu, Z. L. (2006). Curcumin and its Analogues as Potent Inhibitors of Low Density Lipoprotein Oxidation: H-Atom Abstraction from the Phenolic Groups and Possible Involvement of the 4-Hydroxy-3-Methoxyphenyl Groups. *Free Radic. Biol. Med.* 40, 526–535. doi:10.1016/j.freeradbiomed.2005.09.008

Cheng, J. H., Wu, W. Y., Liu, W. S., Chang, G., Liu, Y. L., Yang, Z. G., et al. (1999). Treatment of 17 Cases of Patients with Primary Liver Cancer with *Curcuma Aromatica* Oil Infused via Hepatic Artery. *Shijie Huaren Xiaohua Zazhi* 7, 92.

Choudhari, S. S., and Kareppa, B. M. (2013). Identification of Bioactive Compounds of *Zingiber Officinale* roscoe Rhizomes through Gas Chromatography and Mass Spectrometry. *Int. J. Pharm. Res. Dev* 5, 16–20.

Choudhury, S. N., Ghosh, A. C., Saikia, M., Choudhury, M., and Leclercq, P. A. (1996). Volatile Constituents of the Aerial and Underground Parts ofCurcuma aromaticaSalisb. From India. *J. Essent. Oil Res.* 8, 633–638. doi:10.1080/10412905.1996.9701031

Chowdhury, J. U., Bhuiyan, M. N. I., and Nandi, N. C. (2008b). Aromatic Plants of Bangladesh : Essential Oils of Leaves and Fruits of Litsea Glutinosa (Lour.) C.B. Robinson. *Bangladesh J. Bot.* 37, 81–83. doi:10.3329/bjb.v37i1.1568

Chowdhury, J. U., Nandi, N. C., Bhuiyan, M. N. I., and Mobarok, M. H. (2008a). Essential Oil Constituents of the Rhizomes of Two Types of *Curcuma Longa* of Bangladesh. *Bangladesh J. Sci. Ind. Res.* 43, 259–266. doi:10.3329/bjsir.v43i2.970

D'Auria, M., Mauriello, G., Racioppi, R., and Rana, G. L. (2006). Use of SPME-GC-MS in the Study of Time Evolution of the Constituents of Saffron Aroma: Modifications of the Composition during Storage. *J. Chromatogr. Sci.* 44, 18–21. doi:10.1093/chromsci/44.1.18

De Oliveira, M. G., Marques, R. B., De Santana, M. F., Santos, A. B., Brito, F. A., Barreto, E. O., et al. (2012). α-Terpineol Reduces Mechanical Hypernociception and Inflammatory Response. *Basic Clin. Pharmacol. Toxicol.* 111, 120–125. doi:10.1111/j.1742-7843.2012.00875.x

De Oliveira, T. M., De Carvalho, R. B., Da Costa, I. H., De Oliveira, G. A., De Souza, A. A., De Lima, S. G., et al. (2015). Evaluation of P-Cymene, a Natural Antioxidant. *Pharm. Biol.* 53, 423–428. doi:10.3109/13880209.2014.923003

De Vos, R. C., Moco, S., Lommen, A., Keurentjes, J. J., Bino, R. J., and Hall, R. D. (2007). Untargeted Large-Scale Plant Metabolomics Using Liquid Chromatography Coupled to Mass Spectrometry. *Nat. Protoc.* 2, 778–791. doi:10.1038/nprot.2007.95

DeSouza, L., Wahidulla, S., and Devi, P. (2010). Antibacterial Phenolics from the Mangrove *Lumnitzera Racemosa*. *Indian J. Mar. Sci.* 39, 294–298.

Dixon, R. A., Gang, D. R., Charlton, A. J., Fiehn, O., Kuiper, H. A., Reynolds, T. L., et al. (2006). Applications of Metabolomics in Agriculture. *J. Agric. Food Chem.* 54, 8984–8994. doi:10.1021/jf061218t

Dosoky, N. S., Satyal, P., and Setzer, W. N. (2019). Variations in the Volatile Compositions of *Curcuma* Species. *Foods* 8, 1–14. doi:10.3390/foods8020053

Dosoky, N. S., and Setzer, W. N. (2018). Chemical Composition and Biological Activities of Essential Oils of *Curcuma* Species. *Nutrients* 10, 10–17. doi:10.3390/nu10091196

Eggink, P. M., Maliepaard, C., Tikunov, Y., Haanstra, J. P. W., Pohu-Flament, L. M. M., de Wit-Maljaars, S. C., et al. (2012). Prediction of Sweet Pepper (Capsicum annuum) Flavor Over Different Harvests. *Euphytica* 187, 117–131. doi:10.1007/s10681-012-0761-6

Esatbeyoglu, T., Huebbe, P., Ernst, I. M., Chin, D., Wagner, A. E., and Rimbach, G. (2012). Curcumin--from Molecule to Biological Function. *Angew. Chem. Int. Ed. Engl.* 51, 5308–5332. doi:10.1002/anie.201107724

Fasola, T. R., Oloyede, G. K., and Aponjolosun, B. S. (2011). Chemical Composition, Toxicity and Antioxidant Activities of Essential Oils of Stem Bark of Nigerian Species of Guava (*Psidium Guajava* Linn.). *EXCLI J.* 10, 34–43. doi:10.17877/DE290R-1133

Ferreira, F. D., Kemmelmeier, C., Arrotéia, C. C., Da Costa, C. L., Mallmann, C. A., Janeiro, V., et al. (2013). Inhibitory Effect of the Essential Oil of *Curcuma Longa* L. And Curcumin on Aflatoxin Production by Aspergillus flavus Link. *Food Chem.* 136, 789–793. doi:10.1016/j.foodchem.2012.08.003

Gopalan, B., Goto, M., Kodama, A., and Hirose, T. (2000). Supercritical Carbon Dioxide Extraction of Turmeric (*Curcuma Longa*). *J. Agric. Food Chem.* 48, 2189–2192. doi:10.1021/jf9908594

Hahm, E. R., Cheon, G., Lee, J., Kim, B., Park, C., and Yang, C. H. (2002). New and Known Symmetrical Curcumin Derivatives Inhibit the Formation of Fos-Jun-DNA Complex. *Cancer Lett.* 184, 89–96. doi:10.1016/S0304-3835(02)00170-2

Hall, R. D. (2006). Plant Metabolomics: From Holistic hope, to Hype, to Hot Topic. *New Phytol.* 169, 453–468. doi:10.1111/j.1469-8137.2005.01632.x

He, X. G. (2000). On-line Identification of Phytochemical Constituents in Botanical Extracts by Combined High-Performance Liquid Chromatographic-Diode Array Detection-Mass Spectrometric Techniques. *J. Chromatogr. A.* 880, 203–232. doi:10.1016/S0021-9673(00)00059-5

Herath, H. M. I. C., Wijayasiriwardene, T. D. C. M. K., and Premakumara, G. A. S. (2017). Comparative GC-MS Analysis of All *Curcuma* Species Grown in Sri Lanka by Multivariate Test. *Ruhuna J. Sci.* 8, 103. doi:10.4038/rjs.v8i2.29

Herebian, D., Choi, J. H., Abd El-Aty, A. M., Shim, J. H., and Spiteller, M. (2009). Metabolite Analysis in *Curcuma Domestica* Using Various GC-MS and LC-MS Separation and Detection Techniques. *Biomed. Chromatogr.* 23, 951–965. doi:10.1002/bmc.1207

Ho, J.-C. (2010). Chemical Composition and Bioactivity of Essential Oil of Seed and Leaf fromAlpinia speciosaGrown in Taiwan. *Jnl Chin. Chem. Soc* 57, 758–763. doi:10.1002/jccs.201000105

Hong, L. (2011). *Radix Linderae* Essential Oil Improving the Immunity Activities and Preventing the Occurrence of Decubitus in Aged People. *J. Med. Plants Res.* 5, 3733–3738. doi:10.5897/JMPR.9001070

Hong, S. L., Lee, G. S., Syed Abdul Rahman, S. N., Ahmed Hamdi, O. A., Awang, K., Aznam Nugroho, N., et al. (2014). Essential Oil Content of the Rhizome of *Curcuma Purpurascens* Bl. (Temu Tis) and its Antiproliferative Effect on Selected Human Carcinoma Cell Lines. *ScientificWorldJournal* 2014, 397430. doi:10.1155/2014/397430

Huhman, D. V., and Sumner, L. W. (2002). Metabolic Profiling of Saponins in *Medicago Sativa* and *Medicago Truncatula* Using HPLC Coupled to an Electrospray Ion-Trap Mass Spectrometer. *Phytochemistry* 59, 347–360. doi:10.1016/S0031-9422(01)00432-0

Ishida, J., Kozuka, M., Tokuda, H., Nishino, H., Nagumo, S., Lee, K. H., et al. (2002). Chemopreventive Potential of Cyclic Diarylheptanoids. *Bioorg. Med. Chem.* 10, 3361–3365. doi:10.1016/S0968-0896(02)00164-5

Jiang, D. Q., Pu, Q. L., Huang, P., Huang, X. M., He, Y. Z., He, C. H., et al. (1989). [Studies on the Chemical Constituents of Curcuma Kwangsiensis]. *Yao Xue Xue Bao* 24, 357–359.

Jiang, H., Timmermann, B. N., and Gang, D. R. (2006). Use of Liquid Chromatography-Electrospray Ionization Tandem Mass Spectrometry to Identify Diarylheptanoids in Turmeric (*Curcuma Longa* L.) Rhizome. *J. Chromatogr. A.* 1111, 21–31. doi:10.1016/j.chroma.2006.01.103

Jiang, S. C., Ge, S. B., and Peng, W. (2018). Molecules and Functions of Rosewood: *Dalbergia stevenson*. *Arabian J. Chem.* 11, 782–792. doi:10.1016/j.arabjc.2017.12.032

Joshi, J., Ghaisas, S., Vaidya, A., Vaidya, R., Kamat, D. V., Bhagwat, A. N., et al. (2003). Early Human Safety Study of Turmeric Oil (*Curcuma Longa* Oil) Administered Orally in Healthy Volunteers. *J. Assoc. Physicians India* 51, 1055–1060.

Kala, A., Noureddine, G., Belkacemi, D., Segni, L., Zellagui, Amar., Samir, H., et al. (2009). Composition of the Essential Oil of *Rhanterium Adpressum* Coss. And Durieu. from Algeria. *Arch. Appl. Sci. Res.* 1, 115–118.

Kanase, V., and Khan, F. (2018). An Overview of Medicinal Value of *Curcuma* Species. *Asian J. Pharm. Clin. Res.* 11, 40–45. doi:10.22159/ajpcr.2018.v11i12.28145

Khan, A., Vaibhav, K., Javed, H., Tabassum, R., Ahmed, M. E., Khan, M. M., et al. (2014). 1,8-cineole (Eucalyptol) Mitigates Inflammation in Amyloid Beta Toxicated PC12 Cells: Relevance to Alzheimer's Disease. *Neurochem. Res.* 39, 344–352. doi:10.1007/s11064-013-1231-9

Koo, H. J., and Gang, D. R. (2012). Suites of Terpene Synthases Explain Differential Terpenoid Production in Ginger and Turmeric Tissues. *PLoS One* 7, e51481. doi:10.1371/journal.pone.0051481

Krup, V., Prakash L, H., and A, H. (2013). Pharmacological Activities of Turmeric (*Curcuma Longa* linn): A Review. *J. Homeop Ayurv Med.* 02, 133. doi:10.4172/2167-1206.1000133

Kulyal, P., Kuchibhatla, L. N., Uma Maheshwari, K., Nirmal Babu, K., Tetali, S. D., and Raghavendra, A. S. (2016). Highly Sensitive HPLC Method for Estimation of Total or Individual Curcuminoids in *Curcuma* Cultivars and Commercial Turmeric Powders. *Curr. Sci.* 111, 1816–1824. doi:10.18520/cs/v111/i11/1816-1824

Kumar, V., Shriram, V., Bhagat, R., Khare, T., Kapse, S., and Kadoo, N. (2019). Phytochemical Profile, Anti-oxidant, Anti-inflammatory, and Anti-proliferative Activities of *Pogostemon Deccanensis* Essential Oils. *3 Biotech.* 9, 31. doi:10.1007/s13205-018-1560-0

Kumazawa, K., Kubota, K., and Masuda, H. (2005). Influence of Manufacturing Conditions and Crop Season on the Formation of 4-Mercapto-4-Methyl-2-Pentanone in Japanese green tea (Sen-cha). *J. Agric. Food Chem.* 53, 5390–5396. doi:10.1021/jf050392z

Kutti Gounder, D., and Lingamallu, J. (2012). Comparison of Chemical Composition and Antioxidant Potential of Volatile Oil from Fresh, Dried and Cured Turmeric (*Curcuma Longa*) Rhizomes. *Ind. Crops Prod.* 38, 124–131. doi:10.1016/j.indcrop.2012.01.014

Ladan, Z., Amupitan, J. O., Oyewale, A. O., Okonkwo, E. M., Ladan, E. O., Odjobo, B., et al. (2011). Chemical Composition and Biological Activity of the Volatile Oils of *Hyptis Spicigera* against *Trypanosoma Brucei* Tbb Found in Northern Nigeria. *Afr. J. Pure Appl. Chem.* 5, 53–58.

Le Gall, G., Colquhoun, I. J., Davis, A. L., Collins, G. J., and Verhoeyen, M. E. (2003). Metabolite Profiling of Tomato (Lycopersicon esculentum) Using 1H NMR Spectroscopy as a Tool to Detect Potential Unintended Effects Following a Genetic Modification. *J. Agric. Food Chem.* 51, 2447–2456. doi:10.1021/jf0259967

Leela, N., Tava, A., Shafi, P. M., John, S. P., and Chempakam, B. (2002). Chemical Composition of Essential Oils of Turmeric (*Curcuma Longa* L.). *Acta Pharm.* 52, 137–141.

Li, S., Yuan, W., Deng, G., Wang, P., Yang, P., and Aggrawal, B. (2011). Chemical Composition and Product Quality Control of Turmeric (*Curcuma Longa* L.). *Topharmcj* 5, 28–54. doi:10.2174/2210290601102010028

Li, W., Wang, S., Feng, J., Xiao, Y., Xue, X., Zhang, H., et al. (2009a). Structure Elucidation and NMR Assignments for Curcuminoids from the Rhizomes of *Curcuma Longa*. *Magn. Reson. Chem.* 47, 902–908. doi:10.1002/mrc.2478

Li, Y., Wo, J. M., Liu, Q., Li, X., and Martin, R. C. (2009b). Chemoprotective Effects of *Curcuma Aromatica* on Esophageal Carcinogenesis. *Ann. Surg. Oncol.* 16, 515–523. doi:10.1245/s10434-008-0228-0

Liang, G., Shao, L., Wang, Y., Zhao, C., Chu, Y., Xiao, J., et al. (2009). Exploration and Synthesis of Curcumin Analogues with Improved Structural Stability Both *In Vitro* and *In Vivo* as Cytotoxic Agents. *Bioorg. Med. Chem.* 17, 2623–2631. doi:10.1016/j.bmc.2008.10.044

Ma, X., and Gang, D. R. (2006). Metabolic Profiling of Turmeric (*Curcuma Longa* L.) Plants Derived from *In Vitro* Micropropagation and Conventional Greenhouse Cultivation. *J. Agric. Food Chem.* 54, 9573–9583. doi:10.1021/jf061658k

Mani, P., and Boominathan, M. (2011). Comparative Studies of the Antimicrobial Activity of Crude Extracts and Factions from *Eugena Caryophyllus* against *Candida Albicans* Isolate from Chronic Disease Affected Patients. *Int. J. Institutional Pharm. Life Sci.* 1, 36–47.

Marchese, A., Arciola, C. R., Barbieri, R., Silva, A. S., Nabavi, S. F., Tsetegho Sokeng, A. J., et al. (2017). Update on Monoterpenes as Antimicrobial Agents: A Particular Focus on P-Cymene. *Materials (Basel)* 10, 1–15. doi:10.3390/ma10080947

Meng, X., Wang, Z., and Lv, H. (2010). Constituents and Bacteriostatic Activity of Volatile Matter from Four Flower Plant Species. *Indian J. Agric. Res.* 44, 157–167.

Metuge, J. A., Nyongbela, K. D., Mbah, J. A., Samje, M., Fotso, G., Babiaka, S. B., et al. (2014). Anti-Onchocerca Activity and Phytochemical Analysis of an Essential Oil from *Cyperus Articulatus* L. *BMC Complement. Altern. Med.* 14, 223. doi:10.1186/1472-6882-14-223

Miquel, J., Bernd, A., Sempere, J. M., Díaz-Alperi, J., and Ramírez, A. (2002). The Curcuma Antioxidants: Pharmacological Effects and Prospects for Future Clinical Use. A Review. *Arch. Gerontol. Geriatr.* 34, 37–46. doi:10.1016/s0167-4943(01)00194-7

Moco, S., Bino, R. J., Vorst, O., Verhoeven, H. A., De Groot, J., Van Beek, T. A., et al. (2006). A Liquid Chromatography-Mass Spectrometry-Based Metabolome Database for Tomato. *Plant Physiol.* 141, 1205–1218. doi:10.1104/pp.106.078428

Mohammed, L. M., M. Salah, T. F., and Qader, K. O. (2017). Chemical Composition and Antifungal Activity of *Mentha Spicata* L. Plant from Sulaimaniyah in Iraq. *Kjar* 2, 52–56. doi:10.24017/science.2017.1.11

Mohiuddin, M., Chowdhury, M. J., Alam, M. K., and Hossain, M. (2012). Chemical Composition of Essential Oil of Four Flavouring Plants Used by the Tribal People of Bandarban hill District in Bangladesh. *Int. J. Med. Aromat. Plants* 2, 106–113.

Mukherjee, P. K., Harwansh, R. K., Bahadur, S., Biswas, S., Kuchibhatla, L. N., Tetali, S. D., et al. (2016). Metabolomics of Medicinal Plants - A Versatile Tool for Standardization of Herbal Products and Quality Evaluation of Ayurvedic Formulations. *Curr. Sci.* 111, 1624–1630. doi:10.18520/cs/v111/i10/1624-1630

Murata, S., Shiragami, R., Kosugi, C., Tezuka, T., Yamazaki, M., Hirano, A., et al. (2013). Antitumor Effect of 1, 8-cineole against colon Cancer. *Oncol. Rep.* 30, 2647–2652. doi:10.3892/or.2013.2763

Muthukumaran, P., Kumaravel, S., and Nimia, N. (2019). Phytochemical, GC-MS and FT-IR Analysis of *Papaver Somniferum* L. *Jpbs* 7, 1–8. doi:10.18231/j.jpbs.2019.001

Nagori, K., Singh, M. K., Alexander, A., Kumar, T., Dewangan, D., Badwaik, H., et al. (2011). *Piper Betle* L.: A Review on its Ethnobotany, Phytochemistry, Pharmacological Profile and Profiling by New Hyphenated Technique DART-MS (Direct Analysis in Real Time Mass Spectrometry). *J. Pharm. Res.* 4, 2991–2997. Available at: http://jpronline.info/article/view/9266/4710.

Nahar, D. L., and Sarker, S. (2007). "Phytochemistry of the Genus Curcuma," in *Turmeric: The Genus Curcuma*. Editors K. Ravindran, P. N., and K. N. Babu (Boca Raton, Florida: & Sivaraman), 71–106.

Nampoothiri, S. V., Philip, R. M., Kankangi, S., Kiran, C. R., and Menon, A. N. (2015). Essential Oil Composition, α-Amylase Inhibition and Antiglycation Potential of *Curcuma aromatica* Salisb. *J. Essent. Oil Bearing Plants* 18, 1051–1058. doi:10.1080/0972060X.2014.908746

Nieman, D. C., Cialdella-Kam, L., Knab, A. M., and Shanely, R. A. (2012). Influence of Red Pepper Spice and Turmeric on Inflammation and Oxidative Stress Biomarkers in Overweight Females: A Metabolomics Approach. *Plant Foods Hum. Nutr.* 67, 415–421. doi:10.1007/s11130-012-0325-x

Nikolova, M. (2006). Infraspecific Variability in the Flavonoid Composition of *Artemisia Vulgaris* L. *Acta Bot. Croat.* 65, 13–18.

Núñez, N., Vidal-Casanella, O., Sentellas, S., Saurina, J., and Núñez, O. (2020). Non-targeted Ultra-high Performance Liquid Chromatography-High-Resolution Mass Spectrometry (UHPLC-HRMS) Fingerprints for the Chemometric Characterization and Classification of Turmeric and Curry Samples. *Separations* 7, 32–13. doi:10.3390/separations7020032

Nurfina, A. N., Reksohadiprodjo, M. S., Timmerman, H., Jenie, U. A., Sugiyanto, D., and Van Der Goot, H. (1997). Synthesis of Some Symmetrical Curcumin Derivatives and Their Antiinflammatory Activity. *Eur. J. Med. Chem.* 32, 321–328. doi:10.1016/S0223-5234(97)89084-8

Ogundare, A. O., and Olajuyigbe, A. O. (2012). Bioactivity Guided Isolation of the Antifungal Components in Sawdust Extracts of *Piptadeniatrum Africanum*, and *Terminalia Ivorensis*. *Malays. J. Microbiol.* 8, 34–41. doi:10.21161/mjm.32611

Okumura, N., Yoshida, H., Nishimura, Y., Kitagishi, Y., and Matsuda, S. (2012). Terpinolene, a Component of Herbal Sage, Downregulates AKT1 Expression in K562 Cells. *Oncol. Lett.* 3, 321–324. doi:10.3892/ol.2011.491

Othman, R., Ibrahim, H., Mohd, M. A., Mustafa, M. R., and Awang, K. (2006). Bioassay-guided Isolation of a Vasorelaxant Active Compound from *Kaempferia Galanga* L. *Phytomedicine* 13, 61–66. doi:10.1016/j.phymed.2004.07.004

Paramasivam, M., Poi, R., Banerjee, H., and Bandyopadhyay, A. (2009). High-performance Thin Layer Chromatographic Method for Quantitative Determination of Curcuminoids in *Curcuma Longa* Germplasm. *Food Chem.* 113, 640–644. doi:10.1016/j.foodchem.2008.07.051

Park, S. Y., and Kim, D. S. (2002). Discovery of Natural Products from Curcuma Longa that Protect Cells from Beta-Amyloid Insult: a Drug Discovery Effort against Alzheimer's Disease. *J. Nat. Prod.* 65, 1227–1231. doi:10.1021/np010039x

Parthasarathy, V. A., and Chempakam, B. (2008). in "*Chemistry of Spices*," in Chemistry Of Spices. Editors V. A. Parthasarathy, B. Chempakam, and T. J. Zachariah (Cambridge: CABI). 1–445. doi:10.4327/jsnfs1949.32.267

Pathania, V., Gupta, A. P., and Singh, B. (2006). Improved HPTLC Method for Determination of Curcuminoids from *Curcuma Longa*. *J. Liquid Chromatogr. Relat. Tech.* 29, 877–887. doi:10.1080/10826070500531417

Peng, H. Y., and Yang, X. E. (2005). Volatile Constituents in the Flowers of *Elsholtzia Argyi* and Their Variation: A Possible Utilization of Plant Resources after Phytoremediation. *J. Zhejiang Univ. Sci. B* 6, 91–95. doi:10.1631/jzus.2005.B0091

Phattanawasin, P., Sotanaphun, U., and Sriphong, L. (2009). Validated TLC-Image Analysis Method for Simultaneous Quantification of Curcuminoids in *Curcuma Longa*. *Chroma* 69, 397–400. doi:10.1365/s10337-008-0893-y

Prasath, D., Kandiannan, K., Leela, N. K., Aarthi, S., Sasikumar, B., and Babu, K. N. (2018). Turmeric. *Hortic. Rev.* 46, 99–184. doi:10.1002/9781119521082.ch3

Rahmatullah, M., Azam, M. N. K., Pramanik, S., Sania, S., Rahman, S., and Jahan, R. (2012). Antihyperglycemic Activity Evaluation of Rhizomes of *Curcuma Zedoaria* (Christm.) roscoe and Fruits of *Sonneratia Caseolaris* (L). *Engl.* Int. J. Pharmtech Res. 4, 125–129.

Raina, V. K., Srivastava, S. K., and Syamsundar, K. V. (2005). Rhizome and Leaf Oil Composition ofCurcuma Longafrom the Lower Himalayan Region of Northern India. *J. Essent. Oil Res.* 17, 556–559. doi:10.1080/10412905.2005.9698993

Ravindran, P. N. (2000). in *Black Pepper: Piper Nigrum*. Editor P. N. Ravindran (London: CRC Press).doi:10.1201/9780203303870

Rufino, A. T., Ribeiro, M., Judas, F., Salgueiro, L., Lopes, M. C., Cavaleiro, C., et al. (2014). Anti-inflammatory and Chondroprotective Activity of (+)-α-Pinene: Structural and Enantiomeric Selectivity. *J. Nat. Prod.* 77, 264–269. doi:10.1021/np400828x

Ruslay, S., Abas, F., Shaari, K., Zainal, Z., MaulidianiSirat, H., et al. (2007). Characterization of the Components Present in the Active Fractions of Health Gingers (*Curcuma Xanthorrhiza* and *Zingiber Zerumbet*) by HPLC-DAD-ESIMS. *Food Chem.* 104 (3), 1183–1191. doi:10.1016/j.foodchem.2007.01.067

Saleh-e-in, M. M., Sultana, A., Husain, M., and Roy, S. K. (2010). Chemical Constituents of Essential Oil from *Anethum Sowa* L. Herb (Leaf and Stem) Growing in Bangladesh. *Bangladesh J. Sci. Ind. Res.* 45, 173–176. doi:10.3329/bjsir.v45i2.5721

Salman, Z., Mohd Azizi, C. Y., Nik Norulaini, N. A., and Mohd Omar, A. K. (2006). "Gas Chromatography /Time-Of-Flight Mass Spectrometry for Identification of Compounds from *Parkia Speciosa* Seeds Extracted by Supercritical Carbon Dioxide," in Proceedings of the 1st International Conference on Natural Resources Engineering & Technology, Putrajaya, Malaysia, July 24–25, 2006, 112–120.

Sasikumar, B. (2005). Genetic Resources ofCurcuma: Diversity, Characterization and Utilization. *Plant Genet. Resour.* 3, 230–251. doi:10.1079/PGR200574

Sathiyabalan, G., Lincy, P., Muthukumarasamyand Mohan, V. (2014). GC-MS Analysis of Bioactive Components of *Petiveria Alliacea* L. Whole Plant (Phytolaccaceae). *Int. J. Pharma Res. Heal. Sci.* 2, 387–392.

Sati, S. C., Sati, N., and Sati, O. P. (2011). Bioactive Constituents and Medicinal Importance of Genus Alnus. *Pharmacogn. Rev.* 5, 174–183. doi:10.4103/0973-7847.91115

Setyaningsih, D., Murti, Y. B., Fudholi, A., Hinrichs, W. L. J., Mudjahid, R., Martono, S., et al. (2016). Validated TLC Method for Determination of Curcumin Concentrations in Dissolution Samples Containing *Curcuma Longa* Extract. *J. Ilmu Kefarmasian Indones.* 14, 147–157.

Sharopov, F., and Setzer, W. (2010). Composition of the Essential Oil of *Achillea Filipendulina* Lam. From Tajikistan. *Der Pharma Chem.* 2, 134–138.

Shishu and Maheshwari, M. (2010). Comparative Bioavailability of Curcumin, Turmeric and Biocurcumax in Traditional Vehicles Using Non-everted Rat Intestinal Sac Model. *J. Funct. Foods* 2, 60–65. doi:10.1016/j.jff.2010.01.004

Simoh, S., and Zainal, A. (2015). Chemical Profiling of *Curcuma Aeruginosa* Roxb. Rhizome Using Different Techniques of Solvent Extraction. *Asian Pac. J. Trop. Biomed.* 5, 412–417. doi:10.1016/S2221-1691(15)30378-6

Singh, G., Kapoor, I. P., Singh, P., de Heluani, C. S., de Lampasona, M. P., and Catalan, C. A. (2010). Comparative Study of Chemical Composition and Antioxidant Activity of Fresh and Dry Rhizomes of Turmeric (*Curcuma Longa* Linn.). *Food Chem. Toxicol.* 48, 1026–1031. doi:10.1016/j.fct.2010.01.015

Singh, G., Singh, O. P., and Maurya, S. (2002). Chemical and Biocidal Investigations on Essential Oils of Some Indian *Curcuma* Species. *Prog. Cryst. Growth Characterization Mater.* 45, 75–81. doi:10.1016/S0960-8974(02)00030-X

Sirat, H. M., and Meng, L. L. (2009). Chemical Components of the Rhizome Oil of *Curcuma Heyneana* Val. *Mjs* 28, 323–328. doi:10.22452/mjs.vol28no3.10

Slavík, J., and Slavíková, L. (1977). Alkaloids of Some Himalayan Species of *Meconopsis* Genus. *Collect. Czech. Chem. Commun.* 42, 132–139. doi:10.1135/cccc19770132

Song, Q., Yang, D., Zhang, G., and Yang, C. (2001). Volatiles from *Ficus Hispida* and Their Attractiveness to Fig Wasps. *J. Chem. Ecol.* 27, 1929–1942. doi:10.1023/a:1012226400586

Srinivasan, K., Sambaiah, K., and Chandrasekhara, N. (2004). Spices as Beneficial Hypolipidemic Food Adjuncts: A Review. *Food Rev. Int.* 20, 187–220. doi:10.1081/FRI-120037160

Srivastava, A. K., Srivastava, S. K., and Syamsundar, K. V. (2006). Volatile Composition ofCurcuma Angustifolia Roxb. Rhizome from central and Southern India. *Flavour Fragr. J.* 21 (3), 423–426. doi:10.1002/ffj.1680

Suksamrarn, A., Eiamong, S., Piyachaturawat, P., and Charoenpiboonsin, J. (1994). Phenolic Diarylheptanoids from *Curcuma Xanthorrhiza*. *Phytochemistry* 36, 1505–1508. doi:10.1016/S0031-9422(00)89751-4

Sundaryono, A., Nourmamode, A., Gardrat, C., Grelier, S., Bravic, G., Chasseau, D., et al. (2003). Studies on the Photochemistry of 1,7-Diphenyl-1,6-Heptadiene-3,5-Dione, a Non-phenolic Curcuminoid Model. *Photochem. Photobiol. Sci.* 2, 914–920. doi:10.1039/b301229h

Suntres, Z. E., Coccimiglio, J., and Alipour, M. (2015). The Bioactivity and Toxicological Actions of Carvacrol. *Crit. Rev. Food Sci. Nutr.* 55, 304–318. doi:10.1080/10408398.2011.653458

Tajidin, N. E. (2012). Chemical Composition and Citral Content in Lemongrass (*Cymbopogon Citratus*) Essential Oil at Three Maturity Stages. *Afr. J. Biotechnol.* 11, 2685–2693. doi:10.5897/ajb11.2939

Tang, J., Li, X., and Han, J. (2012). Analysis of Volatile Components in Rhizome Zingibers, *Zingiber Officinale* Roscoe and *Ginger Pee* by GC-MS and Chemometric Resolution. *J. Chin. Med. Res. Dev.* 1, 47–53. doi:10.9754/journal.wmc.2010.00662

Tetali, S. D., Acharya, S., Ankari, A. B., Nanakram, V., and Raghavendra, A. S. (2021). Metabolomics of *Withania Somnifera* (L.) Dunal: Advances and Applications. *J. Ethnopharmacol.* 267, 113469. doi:10.1016/j.jep.2020.113469

Tian, Y., Xu, W., Zhu, C., Lin, S., Li, Y., Xiong, L., et al. (2011). Lathyrane Diterpenoids from the Roots of *Euphorbia Micractina* and Their Biological Activities. *J. Nat. Prod.* 74, 1221–1229. doi:10.1021/np2001489

Tisserand, R., and Young, R. (2013). *Essential Oil Safety-E-Book: A Guide for Health Care Professionals*. Churchill Livingstone, London: Elsevier Health Sciences.

Umar, N. M., Parumasivam, T., Aminu, N., and Toh, S. M. (2020). Phytochemical and Pharmacological Properties of *Curcuma Aromatica* Salisb (Wild Turmeric). *J. App Pharm. Sci.* 10, 180–194. doi:10.7324/JAPS.2020.1010018

Usman, L., Hamid, A. A., George, O., Ameen, O., Muhammad, N. O., Zubair, M., et al. (2009). Chemical Composition of Rhizome Essential Oil of *Curcuma longa* L. growing in Growing in North Central Nigeria. *World J. Chem.* 4, 178–181.

Venkataramani, M., and Chinnagounder, S. (2012). Preliminary Phytochemical Screening and GC-MS Profiling of *Hiptage Benghalensis* (L .) Kurz. *J. Pharm. Res.* 5, 2895–2899.

Wang, P., Liang, W., Kong, C., and Jiang, Y. (2005). Allelopathic Potential of Volatile Allelochemicals of *Ambrosia Trifida* L. On Other Plants. *Allelopath. J.* 15, 131–136.

Yang, S. A., Jeon, S. K., Lee, E. J., Im, N. K., Jhee, K. H., Lee, S. P., et al. (2009). Radical Scavenging Activity of the Essential Oil of Silver Fir (*Abies alba*). *J. Clin. Biochem. Nutr.* 44, 253–259. doi:10.3164/jcbn.08-240

Yuan, C., Nan, P., Shi, S., and Zhong, Y. (2003). Chemical Composition of the Essential Oils of Two Chinese Endemic Meconopsis Species. *Z. Naturforsch C J. Biosci.* 58, 313–315. doi:10.1515/znc-2003-5-603

Zellagui, A., Gherraf, N., and Rhouati, S. (2012). Chemical composition and antibacterial activity of the essential oils of *Ferula vesceritensis* Coss et Dur. leaves, endemic in Algeria. *Org. Med. Chem. Lett.* 2, 31. doi:10.1186/2191-2858-2-31

Zeng, J. H., Xu, G. B., and Chen, X. (2009). Application of the Chromatographic Fingerprint for Quality Control of Essential Oil from GuangXi *Curcuma Kwangsiensis*. *Med. Chem. Res.* 18, 158–165. doi:10.1007/s00044-008-9115-2