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A recent review on developed analytical methods for detection of curcumin

Shivani Pannu
Assistant Professor
School of pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab- 147203
Email: shenupannu70@gmail.com

Mohita Thakur
Assistant Professor
School of pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab- 147203
Email: mohitathakur365@gmail.com

Dr. Puja Gulati*
Professor
School of pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab- 147203
Professor & Principal, School of Pharmacy, Desh Bhagat University, Mandi, Gobindgarh, Fatehgarh Sahib,Punjab
*Corresponding author email: puja_duggal@yahoo.co.in

Mohit Kumar
Ph.D Research Scholar, Mohit Kumar
Department of Pharmaceutical sciences & Technology, Maharaja Ranjit Singh Punjab Technical University, Bathinda, Punjab-151001
Email: maddysharma3303@gmail.com

Dishant Dhingra
M. Pharm
Department of Pharmaceutical sciences & Technology, Maharaja Ranjit Singh Punjab Technical University, Bathinda, Punjab-151001
Email: dhingradishant3@gmail.com

Arzoo Pannu
Ph.D Research Scholar
School of Pharmaceutical sciences, Delhi Institute of Pharmaceutical Sciences and Research, New Delhi-017
Email: arzoopannu@gmail.com

Abstract---Curcumin is a natural yellow pigmented phytoconstituent isolated from the powdered rhizome of Curcuma longa linn belongs to family Zinzieberacea. Curcuma longa linn is commonly known as

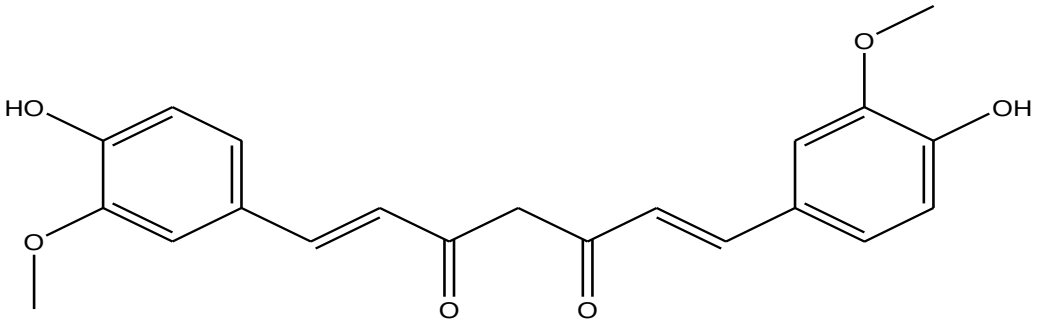
turmeric (Haldi), a well-known Indian spice used as a traditional medicine from ancient era. In literature, there are different analytical methods for detection of curcumin such as HPLC, UPLC and LC-MS/MS. It contains a mixture of different phytoconstituents, therefore it is problematic to separate, identify and isolate pure curcumin from Curcuma longa linn. Hence, in the present review article we have tried to summarize the important analytical parameters required to analyze the curcumin compound in Curcuma longa linn. as it can help the authors to find out best readings to for identification and isolation of curcumin. This review gives a combined study of various analytical methods used for detection of curcumin with retention time, methods used, column used, wavelength, LOD, LOQ etc using different types of well-established HPLC, LCMS, UPLC methods which can be used for isolation, identification and quantitative estimation of curcumin in Curcuma longa linn.

Keywords---Curcumin, HPLC, UPLC, LC-MS, Turmeric

Introduction

Curcumin ((1,7-bis (hydroxyl-3-methoxyphenyl) -1,6-heptadiene-3,5-dione) is a natural yellow pigmented phytoconstituent isolated from the powdered rhizome of *Curcuma longa* linn (Family: Zinzieberacea) (Robinson et al., 2005). *Curcuma longa* linn is commonly known as turmeric (Haldi), which is a well-known Indian spice used as a medicine from ancient era. It has been recorded as precious medicinal spice in Ayurvedic and Unani system of medicine. It is cultivated in tropical and sub-tropical regions around the world but India is the largest producer of turmeric in the world (93.7% of total world production) and is cultivated in 150,000 hectares in India (Phukan et al., 2015). *Curcuma longa* contains different types of curcuminoids, out of which curcumin is reported as the most bio-active compound. These curcuminoids majorily contains 75% curcumin (curcuminI), 20% desmethoxycurcumin (curcuminII), 5% bisdesmethoxycurcumin (curcumin III), essential oils (2-4%), fixed oils (2-3%) (Jayaprakasha et al., 2002) and various volatile oils, including turmerone, atlantone, and zingiberone (Nair et al., 2021). It also contains sugars, proteins and resins.

In 1815, curcumin was isolated from *curcuma longa* for the first time and the characterization was done in 1870. In 1910, the structure of curcumin was elucidated for the first time by Polish scientists. Basically, curcumin is represent to 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione, which is referred as “curcumin I”, having molecular formula $C_{21}H_{20}O_6$, molecular weight of 368.39 g/mol and melting point 183°C. In addition to “curcumin I”, there are two more compounds known as curcumin, which are curcumin II [demethoxycurcumin, 1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)-1,6-heptadiene-3,5-dione] and curcumin III [bisdemethoxycurcumin, 1,7-bis(4-hydroxyphenyl)-1,6-heptadiene-3,5-dione].



(1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione
Curcumin

The various pharmacological activities of curcumin have been evaluated by many researchers around the world. Curcumin has been found as a significant therapeutic agent due to its great medicinal properties and is currently under clinical trials for treating various conditions i.e. pancreatic cancer, multiple myeloma, colon cancer, psoriasis, oral cancer, mastitis myelodysplastic syndromes, diabetes, alzheimer's disease, periodontal disease, pre-cancerous ulcer, recurrent apthous stomatitis, and many other conditions etc. Traditionally, it has been used to treat a variety of illness, including hepatic disorders and jaundice, anorexia, rheumatism, and diabetic ulcers. As a polyphenolic compound, it exerts its pharmacological actions via modulating different signalling pathways and biological processes, resulting in antioxidant, anti-inflammatory, antibacterial, immunomodulatory, neuroprotective, anticarcinogenic, vasodilatory, chemoprotective, and antihyperglycemic potentials as shown in Fig. 1.

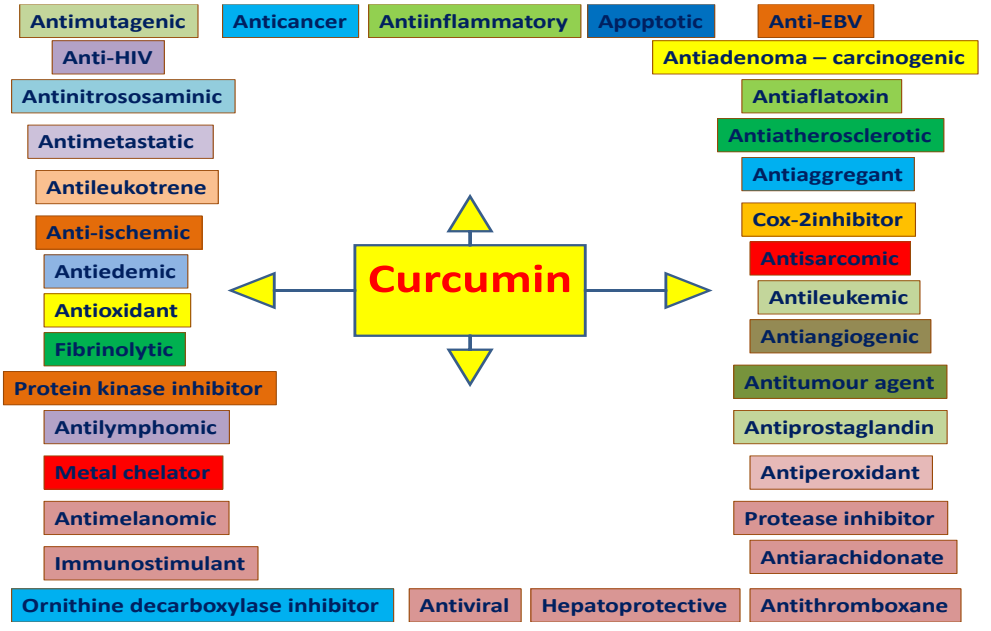


Fig. 1: Pharamcological activities of curcumin

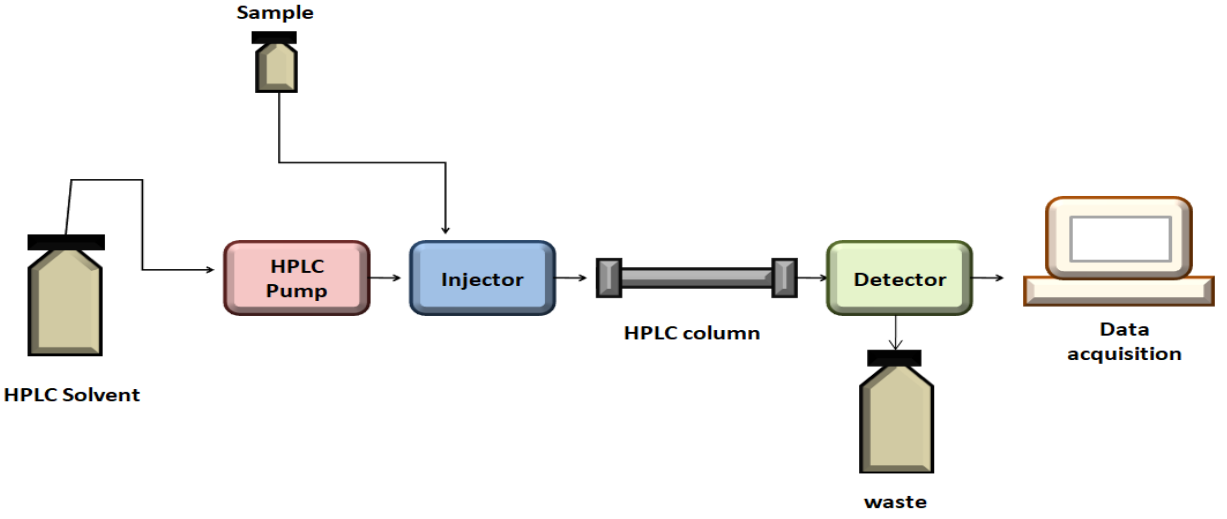
Curcumin has been characterized as safe by the food and drug administration (FDA) USA, the Natural Health Product Directorate of Canada and the Joint FAO/WHO committee on food additives of the Food and Agriculture Organization/World Health Organization. The average intake of curcumin in Indian diet is approximately 2-2.5 g for 60 Kg individual, which corresponds to a daily intake of approximately 60-100 mg of curcumin (Goel et al., 2008).
The chemical formula of curcumin is 1,7-bis-(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-2,5-dione with molecular formula $C_{21}H_{20}O_6$ and its pK_a value of 8.54. Curcumin predominately resides in its keto-form in acidic and neutral conditions and solid phase. It is reported that the maximum absorption (λ max) of curcumin in methanol occurs at 430 nm (Ansari et al., 2005).

The chemical structure of curcumin makes it less soluble in water at acidic and neutral pH but soluble in methanol, ethanol, dimethyl sulfoxide (DMSO) and acetone. It is a hydrophobic polyphenol and several studies have revealed extremely low water-solubility, low stability, rapid metabolism and poor absorption of these molecules that severely reduces its bioavailability (Mohanty et al., 2012). To overcome the problems, several drug delivery systems have been taken into consideration to provide longer circulation times and increased permeability.

Various HPLC, HPTLC, UPLC, LCMS/MS methods have been reported for the determination of curcumin in various sample matrixes. HPLC analysis of curcumin was first attempted by (Asakawa et al., 1981) using Nucelosil C18 column as stationary phase, a mixture of Acetonitrile: H2O: Acetic acid (51: 49: 5) as mobile phase and benzyl benzoate as an internal standard. Many HPLC methods have been reported since then. These methods varied depending of different types of matrix, objective of analysis, sensitivity, detector and column used. For a particular HPLC analysis for curcumin, analyst should select chromatographic parameters judiciously based on earlier published methods. So, the objective of this review article is an in-depth analysis of published HPLC articles that will be useful to the readers for selection of various chromatographic parameters for their study.

Method

Reported HPLC Methods
The Chromatogrphy method was performed for extract as per the method was reported in labs.



2.1. HPLC Instruments

Various type of HPLC instrument companies like Shimadzu HPLC instrument-LC-20AD (Japan) equipped with Rheodyne 7725i injection valve with a 20 µL loop volume and Binary gradient pump, Plus Intelligent LC pump PU-2080 from Jasco (Tokyo, Japan) equipped with a Jasco UV-2075 Intelligent UV/Vis detector and a Rheodyne 7725 injector (Rheodyne, Cotati, CA, USA), A Waters 2695 Alliance HPLC system (Milford, MA, USA), A Agilent 1100 separation module with a photodiode array detector, A Varian® ProStar HPLC system, Agilent quaternary system with 1260 quat pump, injector, variable wavelength detector 1260 VWD VL and auto sampler 1260 ALS, Waters 625LC HPLC system.

*2.*2. Selection of Column

Various Columns are used in the HPLC system i.e. RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg) (Kadam et al., 2018), Algilent RPC18XDB column(4.6*150mm) (Wulandari et al., 2018), 25cm*4.6mm i.d. stainless steel analytical 5mm particle LiChrosphere-100 RP 18 packing column (Chaudary Hema et al.) , Waters Symmetry Shield (3.9*150 mm) (A.RAdha et al.), 5µm C_{18} , AlltactAlltima C_{18} Column (150*4.6 mm) (Wichitnithadwisut et al.), Thermo Hypersil Gold column (250 mm × 4.6 mm I.D.: 5 µm) (Ang Fung Lee et al.).

2.3 Selection of Mobile phase

There are various mobile phases are used in the Hplc system i.e Acetonitrile:Acetic acid (49:51 v/v) (K.Prabaning dyah Niken et al.), Acetonitrile:Acetic acid (50:50 v/v) (Wulandari et al., 2018), Ethanol:Water:Acetonitril (80:10:10 v/v/v) (Thuane Castro Frabeldo Nascimen et al.), Ortho phosphoric acid: acetonitrile (65:35) (Chaudary Hema et al.), Aqueous acetic acid: methanol (15:85v/v) (Cheng et al., 2010) Acetonitril:Tetrahydrofuran:Water (35:20:45 v/v/v) (Han Yangrui et al.), Acetonitrile:water (60:40 v/v) (Hu liandong et al.), Acetonitril:Acetic acid (55:45 v/v) (A.Radha et al.), KH_2PO_4:Methanol (65:35 v/v) (A.Koray Mohamed et al.), Acetonitril:Methanol:Water (40:20:40 v/v/v) (Khalid Syed Haraaon).

2.4 Selection of Detector

These are various Detectors are used for the determination of Curcumin and their other constituents. These detectors are Jasco UV-2075 Intelligent UV/Vis detector, UV spectrophotometer, detector PDA,Detector (Waters 2998) and a fluorescence detector (Waters 2475), a ProStar 330 UV-Vis PDA spectrophotometric detector,Waters 2487 dual channel UV detector,9050 UV visible Detector, detector 1260 VWD VL,Photodiode array detector, Waters 486 tunable absorbance detector,UV vis dual wavelength spectrophotometric detector (SPD-10AVP).

Mobile Phase	Column	Detection	Retention time	LOD	LOQ	Reference
Ammonium acetate in water (pH-3): Acetonitrile (100%)	RP18 Water® X-Bridge (250*4.6mm i.d.; 5µm)	424nm	NA	2.23 µg/mL	6.774 µg/mL	(Kadam et al., 2018)
Acetonitrile:Aceticaci (49:51 v/v)	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg)	425 nm	NA	0.056 µg/mL	0.169 µg/mL	(Prabaningdyah et al., 2017)
Acetonitrile: Acetic acid (50:50 v/v)	Algilent RPC18XDB column(4.6*150mm	425 nm	NA	0.004µg/mL	0.016 µg/mL	(Wulandari et al., 2018)
Water: Acetonitrile	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg)	254 nm	NA	0.3 µg/ml and 0.03 µg/ml	1 µg/ml and 0.1 µg/ml	(Gugulothu & Patravale, 2012)
Ethanol:Water: Acetonitril (80:10:10 v/v/v)	Algilent RPC18XDB column(4.6*150mm	250 nm	0.96, 1.26, and 1.36 min	9.65 ng/ml	50 ng/ml	(Castro Frabel do Nascimento et al., 2012)
Ortho phosphoric acid: acetonitrile (65:35)	25cm*4.6mm i.d. stainless steel analytical 5mm particle LiChrosphere-100 RP 18 packing column containing	425 nm	13.09+/-1.01	245.5 55.30 ng/ml	491.1 165.87 ng/ml	Chaudhary et al .
Acetonitril:Water (50:50 v/v)	Stainless steel analytical 5mm particle LiChrosphere-100 RP 18 packing column containing	425 nm	13.6, 12.1 and 10.8 min	11.61 ng/ml	500 ng/ml 5 and 10 ng/ml	(Fonseca-Santos et al., 2017)
Aqueous acetic acid: methanol (15:85v/v)	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg) 25cm*4.6mm i.d.	420 nm	8.7 min	40.66, 49.38,29.28 pg.	134.18, 164.44, 97.50 pg	(H. Chen et al., 2009)
Acetonitril:Tetrahydrofuran:Water (35:20:45 v/v/v)	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg)	425 nm	6.5,11.5,19.9 mins	NA	5 & 10 ng/ml	(Han et al., 2011)
Acetonitril:Methanol:Deionizedwater:Acetic acid (41:23:36:1 v/v/v/v)	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg)	262 nm	NA	0.091 µg/ml	NA	(Heath et al., 2003)
Acetonitrile:water (60:40 v/v)	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg)	428 nm	NA	NA	NA	Hu liandong et.al
Acetonitril:Acetic acid (55:45 v/v)	Waters Symmetry Shield (3.9*150 mm),5µm C_{18}	425 nm	0.176	0.356,1.80,0.074 ppm	1.078,5.545,0.224 ppm	(Radha et al., 2016)
KH_2PO_4:Methanol (65:35 v/v)	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg)	288 nm	55 mins	0.0031,0.0035 µg/ml	0.0104, 0.0118 µg/ml	Koray Mohamed et.al
Acetonitril:	Waters	300 & 428	8.6 & 5.9 min	20 ng/ml	NA	Mazengshuan et.al

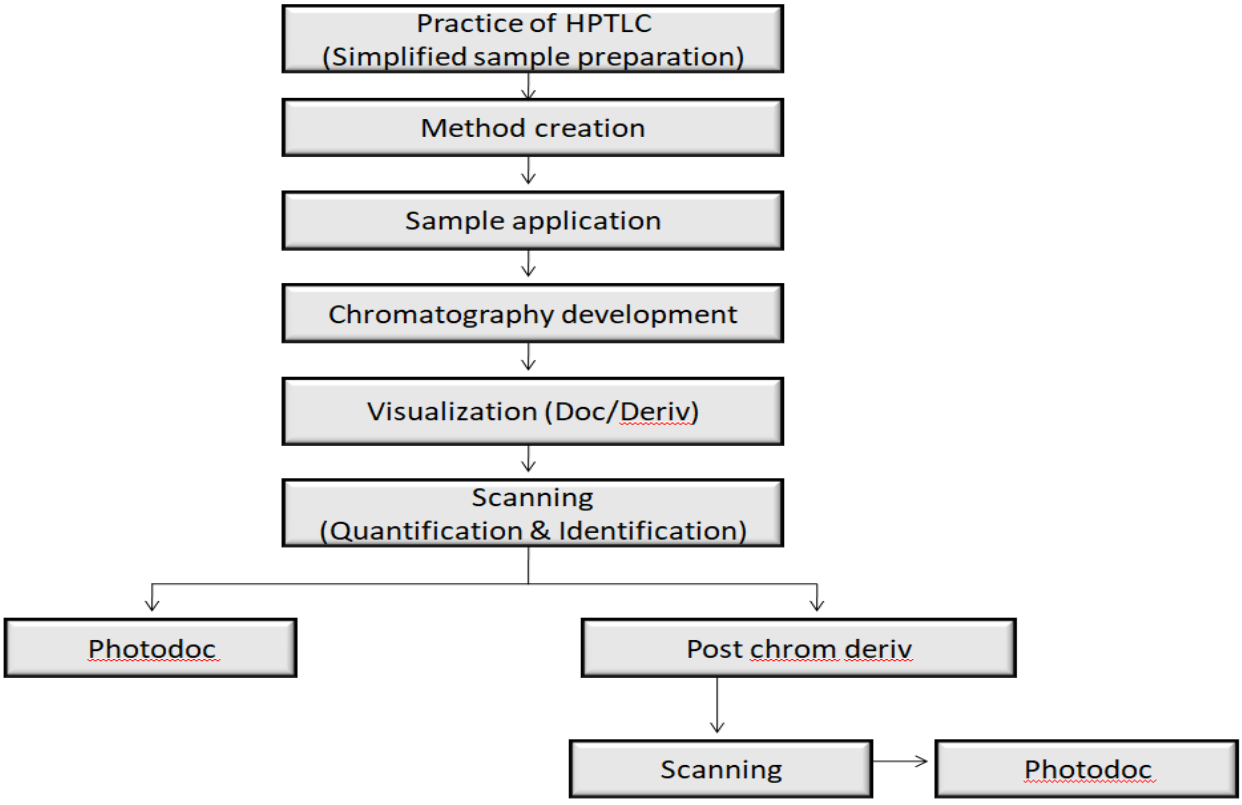
Citric buufer (55:45)	SymmetryShield 3.9*150 mm,5µm C_{18}	nm				
Acetonitril: Water or Chloroform: Methanol	Waters µBondapok™ C_{18} (3.9 *300 mm)	265 nm	**NA**	2.5 ng/ml	NA	Indira PriyadarsiniKavirayani
Chloroform:Methanol (48:2 v/v)	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg)	425 nm	NA	0.1 µg/spot	NA	(Paramasivam et al., 2008)
Aetonitril:Methanol (20:50 v/v)	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg)	332 nm	2.8 +/- 0.2, 5.1 +/-0.2 mins	NA	0.167,0.271 µg/ml	(Rathore et al., 2008)
Acetonitril:Methanol:Water (40:20:40 v/v/v)	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg)	370 nm	6.728,6.166,5.66 mins	0.305 µg/ml	2 µg/ml	Khalid Syed Haraaon
Acetonitril:Formic acid (60:40 v/v)	RP18 Water® X-Bridge(250*4.6mm i.d.;5mcg)	NA	5.90,6.64,6.33 mins 13.6,12.1,10.8 mins	NA	1,0.50 ng/ml	Wang XIu-Mei et.al
Acetonitril:Acetic acid (40:60 v/v)	AlltactAlltima C_{18} Column (150*4.6 mm)	425 nm	NA	0.90,0.84,0.08 µg/ml	2.73,2.53,0.23 µg/ml	WichitnithadWisut et.al
Acetonitrile: Acetic acid (40:60)	Thermo Hypersil Gold column (250 mm × 4.6 mm I.D.: 5 µm)	370 nm	32.195, 2.887 and 2.830	0.00488, 0.62500, 0.07813 and 0.03906 µg/mL	0.03906, 2.5000, 0.31250 and 0.07813 µg/mL	(Ang et al., 2014)

Later on, Tonnesen et al. reported a HPLC method which was able to separate three different components of curcuminoids. There are different detectors were used based on UV-Vis and on fluorescence. The fluorosence detector showed sensitivity that was 0-fold higher than the UV-Vis detector in detecting three components of curcuminoids (Curcumin,demethoxycurcumin, and bis – desmethoxycurcumin). The five different eluents (combination of EtOH-water, MeOH-water, and butanol) as well as eight stationary phases were evaluated. It was found that the 1,3-diketone group in curcuminoids was adsorbed strongly to the salicyclic acid column, hence the analysis was not reproducible.

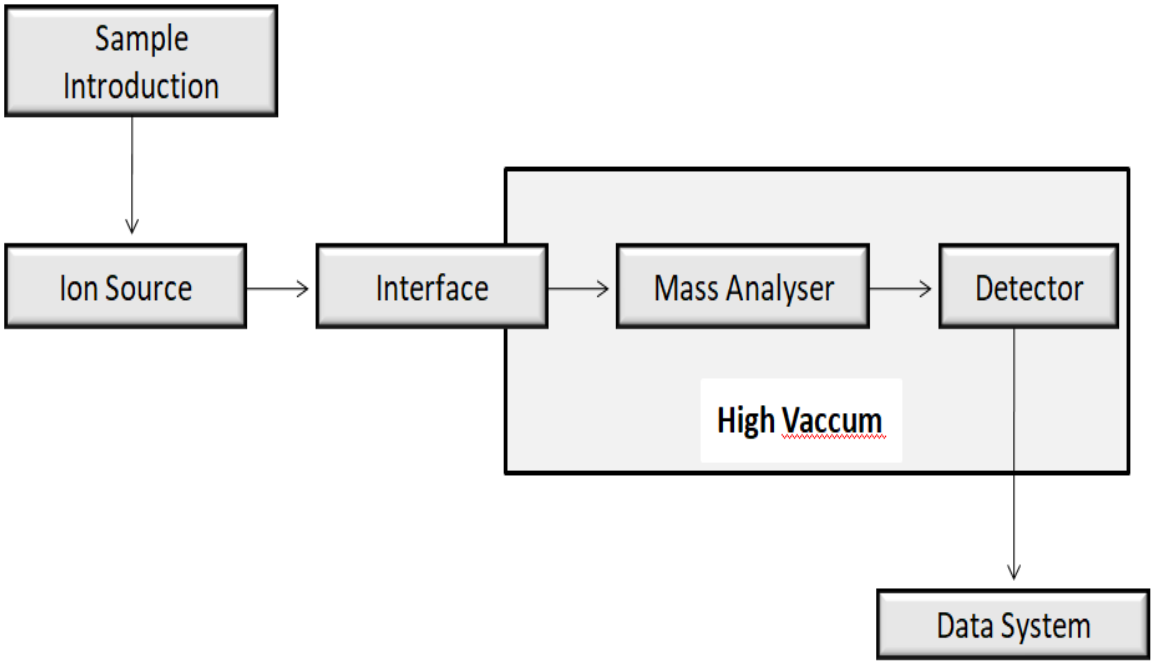
Mobile Phase	Column	Detection	Retention time	LOD	LOQ	Reference
Tlouene:chloroform: methanol (5:4:1 v/v/v) 180	TLC Aluminium Plates Precoated with a silica gel $60F_{254}$	NA	NA	50 ng/ml	200 ng/ml	(Ashraf et al., 2012)
N-hexane:ethylacetate: aceticacid:methanol (7:2:0.5:0.5 v/v/v/v)	Precoated TLC silica gel aluminium plates 60 F_{254} (20*10 cm),250µm thickness	404 nm	30 mins	18.31and 40.50ng/spot	55.50 and 122.74 ng/spot	(Kharat et al., 2017)
Toluene:Ethylacetate :Methanol (8:1:1 v/v/v)	TLC Aluminium Plates Precoated with a silica gel $60F_{254}$	293 nm	20 mins	26,31,29 ng/band	77,92,88 ng/band	(Siddiqui, 2015)
Dichloromethane: Methanol(99:1)	Precoated TLC silica gel aluminium plates 60 F_{254} (20*10 cm),250µm thickness	427 nm	NA	49 ng/spot	148 ng/spot	(Gantait et al., 2011)
Chloroform:Ethanol: Acetic Acid (95:4:5 v/v/v)	Precoated TLC silica gel aluminium plates 60 F_{254} (20*10 cm),250µm thickness	288 nm	10 mins	NA	NA	Srivastava et.al
Toluene: Ethylacetate: Formic acid (9:6:0.4 v/v/v)	TLC Aluminium Plates Precoated with a silica gel $60F_{254}$	200-700 nm	NA	NA	NA	N.TahaMahamoud et.al
Chloroform: Methanol (9.5:0.5)	Precoated Silica gel $60F_{254}$ Aluminium Plates(10*20cm)	421nm	NA	8ng/spot	25ng/spot	(Kandasamy & Moscow, 2013)
n-hexane:ethyl acetate:methanol: formic acid (8:2:1:2-3 drops v/v)	Precoated with silica gel 60F254 aluminium plates	421nm	NA	27.3ng	82.7ng	(Kekre & Walode, 2012)
Chloroform:ethyl acetate:formic acid:methanol (7.5:6:0.5:0.5)	Aluminium plates precoated with silicagel 60F254(20*10cm) thickness 0.2 mm	322nm	NA	29ng	75ng	(Chavan et al., 2015)
Chloroform: methanol (48:2 v/v)	Glass backed silica gel 60GF254 (20*20cm) thickness 300µ	425nm	NA	NA	NA	(Paramasivam et al., 2008)
Chloroform: methanol (9:1)		420nm	NA	17.39ng/spot	52.71ng/spot	(Dixit et al., 2008)
Chloroform:methanol :glacial acetic acid (7:2:0.3)	Precoated with silica gel 60F254	366nm	NA	NA	NA	(Mishra et al., 2017)
Chloroform: ethyl acetate:formic acid (7.5:6:0.2)	Aluminium plates precoated with silica gel 60F254	540nm	NA	0.06ng/spot	0.2 ng/spot	(Vaykole et al., 2014)
Chloroform: methanol (98:2 v/v)	Lichro-sphere aluminium plates Si 60F254 (20*20cm)	366nm	NA	40ng	100ng	(Pathania et al., 2006)
Toluene:ethyl acetate: formic acid (4.5:3:0.2)	Silica gel 60 F254 percolated TLC plate (10*10cm) thickness 0.2mm	366nm	NA	16ng/spot	53.34 ng/spot	(Thakker et al., 2011)

Chloroform: ethyl acetate: formic acid (7.5:6:0.5)	Silica gel 60F254 TLC plates (20*10cm) thickness 0.2mm	254nm	NA	100ng/spot	300ng/spot	(Sonawane et al., 2011)
Toluene: ethyl acetate: methanol	Silica gel 60F254 HPTLC Plates	420nm	NA	25ng	NA	(J. K. Verma & Joshi, 2006)
Chloroform: methanol (9.25:0.75 v/v)	TLC aluminium plates precoated with silica gel 60F254	430nm	NA	8ng/spot	25ng/spot	(Ansari et al., 2005)
Toluene: ethyl acetate: methanol (8:1:1 v/v/v)	Precoated HPTLC Plates (20*10cm)	293nm	NA	26ng/band	77ng/band	(Siddiqui, 2015)

HPTLC method



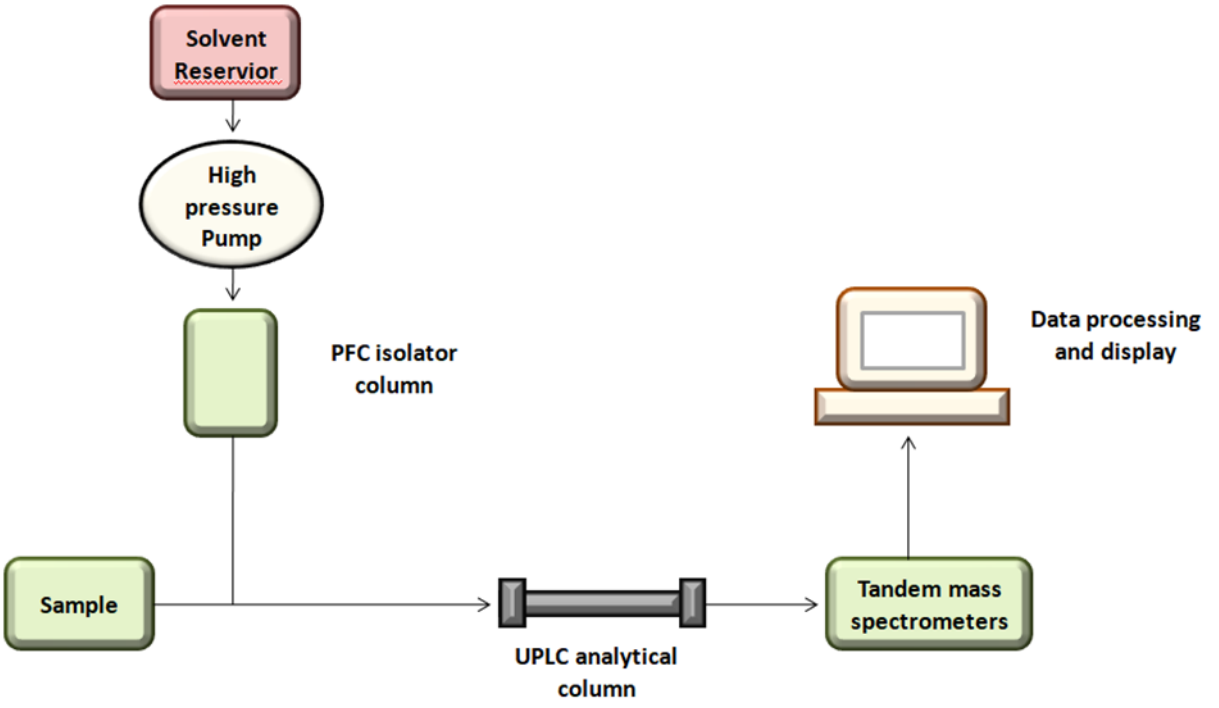
LC-MS/MS method



Mobile Phase	Column	Detection/ Ion Transition	Retention time	LOD	LOQ	Reference
Acetic acid: Acetonitrile	ZorbaxEclpise C_{18} (4.6*150 mm)	425 nm	8.2 ± 0.2 min and 1.4 ± 0.1 min	NA	10 ng/ml	DalapathiGugulothu et.al.pdf.in
Mehanol: Ammonium Acetate (80:20 v/v)	ZorbaxEclpise C_{18} (4.6*150 mm)	230 nm	30 mins	0.01, 0.25 µg/ml	0.4,1.2 µg/ml	Memvanga Patrick et.al
Acetonitrile: 1mM Formic Acid (70:30 v/v)	Reverse phase c18 column (150*46mm) Zorbax	367-217 m/z	NA	1ng/ml	5ng/ml	(Yang et al., 2007)
Acetonitrile : water (70:30 v/v)	C18 phenomenex luna, 250mm*4.6mm	372-137 m/z	NA	NA	0.5ng/ml	(Liu et al., 2006)
Methanol:10mM Ammonium Formate(ph 3.0) (1:1)	Waters MS C18 column (2.1mm* 50mm, 3.5µm)	367-149 m/z	5.08 mins	NA	2.50ng/ml	(Kunati et al., 2018)
	Phenomenex Luna silica column (50mm*4.6mm* 5µm)	369-245 m/z	NA	1µg/l	10µg/l	(Gören et al., 2009)
0.1% Formic acid in water: Acetonitrile (15:85) (5:95) (25:75)	Agilent zorbax eclipse* DB C 18 column (3.5µm, 4.6*50 mm)	369-245-213 m/z	2.5min	0.1ng/ml	1ng/ml	(Li et al., 2018)
0.2% Formic acid : Acetonitrile (50:50)	Gilent poroshell SB C18(2.7µm, 4.6*150mm)	369-179 m/z	1.5min	0.5ng/ml	1ng/ml	(Z. Chen et al., 2017)
Acetonitrile: 0.2% formic acid (73:27 v/v)	Halo C18 column (2.7µm, 4.6*50mm)	369-177 m/z	1.5min	NA	1ng/ml	(Bhuket et al., 2016)
Acetonitrile: 0.1 formic acid (95:5) (5:95)	C18 column (100mm*2.1mm, 1.7µm)	369-177 m/z	4.1min	NA	5ng/ml	(Ma et al., 2015)
Acetonitrile: 0.1% formic acid (50:50) v/v	Sepax BR-C18 (5µm,1.0*100mm)	369-285 m/z	2.2 min	NA	2.5ng/ml	(Ramalingam & Ko, 2014)
50%Acetonitrile: 0.1% formic acid (1:1)	Thermo Beta Basic C8 column (5µm, 2.1*50mm)	369-177 m/z	NA	1ng/ml	2ng/ml	(Cao et al., 2014)
0.1% formic acid with water: 1% formic acid with Acetonitrile (50:50) v/v	C8 column (2.1*50mm, 5µm)	425nm 545-351m/z	NA	NA	NA	(Zhongfa et al., 2012)

Acetonitrile: 10mM ammonium acetate buffer(ph 3.5) (8:20) v/v	Chromolith C18 (50mm*4.6, 5µm)	367-217 m/z	NA	NA	NA	(Kakkar et al., 2010)
Methanol: 0.05% acetic acid (80:20)	C18 100A column (250mm*4.6mm *5µm)	369.3-285 m/z	1.08min	NA	0.5ng/ml	(Khalil et al., 2013)
100% Methanol: 0.2% formic in water (ph 2.5) (10:90) (90:10)	Synergi™ Fusion-RP C18	NA	1.5min	NA	NA	(Bangphumi et al., 2016)

UPLC method



Mobile Phase	Column	Detection	Retention time	LOD	LOQ	Reference
Aqueous phosphoric acid:Acetonitril (34:66v/v)	Water Acquity® BEH C_{18}, h_{55}BEH C_{18}, h_{ss} T_3 & BEH Shield RPC_{18} BEH RP_{18} (2.1&100 nm)	420 nm	1.576,1.435,1.30 mins	NA	NA	(Cheng et al., 2010)
5% Aqueous Acetonitril: Acetic Acid &Acetonitril	Water Acquity® BEH C_{18}, h_{55}BEH C_{18}, h_{ss} T_3 & BEH Shield RPC_{18} BEH RP_{18} (2.1&100 nm)	426 nm	NA	2.5 ng/ml	NA	H.Marczylo Timothy et.al
2% v/v acetic acid in water: Acetonitrile (55:45) (20:80)	C18(1.7µm, 2.1*50mm)	400nm	1.8min	0.050µg/ml	0.075µg/ml	(Bhuket et al., 2020)
Acetonitrile: water	UPLC BEH C18 (1.7µm, 2.1*50mm)	360nm 435nm	NA	0.008ng/ml 0.003ng/ml	0.02ng/ml 0.01ng/ml	(Cui et al., 2017)
0.05% aqueous phosphoric acid: Acetonitrile (36:66) v/v	BEH Shield RP C18 (2.1*100mm, 1.7µm)	420nm	NA	40.66pg	134.18pg	(Cheng et al., 2010)
Acetonitrile:	C18	NA	NA	NA	NA	(Jude et al.,

Methanol with 10mM ammonium formate in water (70:30)	(2.1*50mm, 1.7µm)					2018)
Acetonitrile : 10mm ammonium formate buffer containing 0.1 % formic acid	BEH HILIC 18 (2.1*100mm, 1.7µm)	NA	NA	NA	NA	(S. Wang et al., 2018)
Formic acid : Acetonitrile (72:28) (10:90)	UPLC® BEH C18 (2.1*50mm, 1.7µm)	369-25 m/z	2.5min	NA	1ng/ml	(Ramadanty et al., 2019)
0.15% Formic acid: Acetonitrile (50:50) v/v	UPLC BEH C18 column 1.7µm, 2.1*100mm)	369-176.95	1.7min	NA	1ng/ml	(Hayun et al., 2018)
0.05% o-phosphoric acid: Acetonitrile (66:34) v/v	HSS-T3 C18 (1.8µm, 2.1*50mm)	425nm	NA	NA	NA	(Saralkar & Dash, 2017)
Acetonitrile: 10mM ammonium acetate buffer	ACQUITY UPLC® BEH C18 (100*2.1mm,	NA	NA	NA	NA	(L. Wang et al., 2019)

(ph-3.5) (85:15) (5:95) (60:40) (75:25) (50:50)	1.7µm)					
10%v/v Acetonitrile in water: Acetonitrile (70:30) (40:60)	ACQUITY UPLC BEH C18 (100*2.1mm, 1.7µm)	NA	NA	NA	NA	(Hocking et al., 2018)
Acetonitrile containing trifluoro acetic acid(0.1% w/v): Water (50:50)	UPLC BEH C18 column (100*2.1mm, 2µm)	425nm	NA	NA	NA	(Xue et al., 2018)
Acetonitrile: 5% Acetonitrile in water with 0.01% acetic acid (75:25) v/v	C18 column (50*2.1mm)	NA	NA	NA	2.0ng/ml	(M. K. Verma et al., 2013)v
Acetonitrile: 10mM ammonium	Waters ACQUITY UPLC BEH	367.0894-217.1410 m/z	2.18min	0.318ng/ml	1ng/ml	(Ashraf et al., 2015)

formate (70:30)v/v	C18 (100*2.1mm, 1.7µm)					
Acetonitrile: 10mMammonium acetate (90:10)v/v	Waters ACQUITY UPLC™ BEH C18 (2.1*100mm, 1.7µm)	367-217.1 m/z	2.18min	NA	NA	(Anwar et al., 2015)
Acetonitrile: 0.1% formic acid with water (80:20)v/v	C18 (50*2.1mm, 3µm)	369-176.9 m/z	NA	NA	1.0ng/ml	(Yu et al., 2019)
0.1% Formic acid : Acetonitriloe (70:30) (25:85)	Waters ACQUITY UPLC™ BEH C18 (2.1*100mm, 1.7µm	NA	NA	NA	NA	(J. Wang et al., 2015)
Acetonitrile: 2mM ammonium acetate (85:15) v/v	ACQUITY UPLC™ BEH C18 (2.1*100mm, 1.7µm	367.08-217.03 m/z	1.72min	0.017ng/ml	0.05ng/ml	(Ahmad et al., 2016)

Conclusion

The present review article has summarized the important parameters required to analyse the curcumin compound in *Curcuma longa* linn., since it contain a mixture of different phytoconstituents, it is problematic to separate, identify and isolate pure curcumin from it. HPLC, LCMS, UPLC are reproducible and versatile

chromatogreaphic techniques for the qualitative and quantitative estimation of any kind of secondary metabolites present in plants. Therefore, in this review, we have concluded that there are different types of well-established HPLC, LCMS, UPLC methods which can be used for isolation, identification and quantitative estimation of curcumin in *Curcuma longa* linn.

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