**ABSTRACT**

Herbal formulation dosage form consists of one or more herbs processed in specified quantities to provide specific nutritional, cosmetic benefits use to diagnose the disease. Herbal formulations contain an active substance and preparation in combination of one or more herbal compounds. *Berberis aristata* is one of herbs of an ancient Ayurveda medicine and different properties along with various treatment of illness. Berberine, is a type of alkaloid which is quaternary protoberberine, is one of the known bioactive compounds scattered extensively in a number of clinically significant medicinal plants such as *Hydrastis canadensis* L., *Phellodendron amurense* R., *Coptis japonica* M., and Berberine containing plants have been used in traditional and folk medicine around the globe for centuries. It has been used for a pyretic diarrhea, bitter tonic, and eye infections. In the past three eras, Berberine has been studied intensively in over thousands cases because of its therapeutics, physicochemical effects, pharmacological, and physiological effects such as cardiovascular, anti-inflammatory, anti leishmanial, and anti-secretory effects. Berberine act as a phytoconstituents in formulations and available in ayurveda, allopathy, and homeopathy medicines. With this review, we will evaluate the various traditional and medicinal use of Berberine and their isolation and extraction procedure. We will also review the potential of this plant as various dosage forms for the treatment of various diseases.

**Keywords:** Berberine; Extraction Method; Isolation method; Skin problems

**INTRODUCTION**

Now-a-days herbal medicines are widely used and recommend for the treatment of patients health care. Herbal formulation dosage form consists of one or more herbs processed in specified quantities to provide specific nutritional, cosmetic benefits use to diagnose the disease. Herbal formulations contain an active substance and preparation in combination of one or more herbal compounds. Herbal formulations are obtained by extraction, distillation, expression, purification, fractionation include powdered of various crude plants.

Herbal formulations are inexpensive, and possess good therapeutic action, better for patients' health care. Herbal formulations have no or less side effects as compared to allopathic or other systems. Herbal Formulation is used in the treatment of medical conditions, enhancement of bioavailability, pharmacological activity and solubility.

Ayurveda is a traditional system and improve physical, mental and emotional support for patients. Ayurveda is an ancient medicine healing system. It was developed more than 3000 years ago in India. Ayurveda helps to improve good health, cure disease, preventing and treating disease illness. Ayurveda believe in five basic elements found in universes such as space, air, fire, water and earth and human body systems supports three life energies or forces are known as doshas. Doshas are known as Vata dosha, Pitta dosha and Kapha dosha each controls in different body systems.

*Berberis aristata* is one of herbs of an ancient Ayurveda medicine and different properties along with various treatment of illness. Berberine is an active phytoconstituents which is available in ayurveda, allopathy, and homeopathy medicines. The whole part of plant is also good source of dye and tannins. Berberine is main chemical constituents having various pharmacological actions. It is an active constituent

**A Laconic Review on Extraction, Biological Activities of Herbal Formulations of Berberine: A Traditional Drug**

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benzylisoquinoline alkaloid and used in Ayurvedic and Chinese systems.\textsuperscript{4,5}

This review evaluates various pharmacological traditional properties of Berberine along with their extractions method and potential use in the treatment of psoriasis and other disease.

### BASIC PROPERTIES AND USE OF BERBERINE

The basic properties of Berberine were shown in Table 1. The chemical structure of Berberine is represented in Figure 1. Berberine has various biological and traditional uses which are listed in the Table 2. Berberine was intensively used in the skin disorders and the whole information regarding their uses in skin disorders are listed in the Table 3.

#### Table 1: Basic properties of Berberine

| Sr. no. | Basic properties                              |
|---------|-----------------------------------------------|
| 1       | Chemical formula: C\textsubscript{20}H\textsubscript{18}NO\textsubscript{4}+ |
| 2       | Molecular mass: 336.366gmol\textsuperscript{-1} |
| 3       | Structure name: 5,6-dihydro-9,10-dimethoxybenzo[g]-1,3-benzodioxolo[5,6-a]quinolinizinium (quaternary amine) |
| 4       | Basic nucleus: Quaternary benzylisoquinoline alkaloid molecule |
| 5       | Nature: Non basic |
| 6       | Appearance: Yellow solid |
| 7       | Melting point: 145°C |
| 8       | Solubility: Poor water soluble |
| 9       | Salt: Water, acidic, neutral media |
| 10      | Base: Soluble in organic solvents |

#### Figure 1: Berberine

![Figure 1](image)

#### Table 2: Biological and traditional uses of plants

| Sr. no. | Biological name | Plant name | Traditional uses |
|---------|-----------------|------------|------------------|
| 1       | Berberis vulgaris | Barberry   | Acne, inflamed bumps, pimples, cardiovascular and hypertension |
| 2       | Argemone mexicana | Prickly poppy | Malaria, jaundice, snake bites |
| 3       | Berberis aristata | Turmeric   | Antibacterial, anti-diarrheal and anticancer |
| 4       | Mahonia aquifolium | Oregon grape | Eczema, tuberculosis, periodontitis, dysentery, wounds |
| 5       | Hydrastis canadensis | Goldenseal | As astringent, bitter tonic, laxative, antidiabetic and muscular stimulant |
| 6       | Eschscholzia californica | Californian poppy | Depression, nerve pain, psychiatric conditions, blood vessel problems and sedation |
| 7       | Xanthorrhiza simplicissima | Yellow root | Anti-inflammatory, astringent, antimicrobial, anticonvulsant and immunostimulant |
| 8       | Phellodendron amurense | Amur cork tree | Osteoarthritis, weight loss and obesity, diarrhea, ulcers in stomach, diabetes, pneumonia, anti-inflammatory activity |
| 9       | Coptis chinensis | Chinese goldthread | Dye, wool and fibers |
| 10      | Tinospora cordifolia | Heart-leaved moonseed | Gout, lymphoma, rheumatoid arthritis, peptic ulcer, cancers and immune system |
In the Berberidaceae family, they used as raw material and an important ingredient used in Ayurvedic traditional medicine and Chinese medicine. Berberis genus includes 450-500 species which represent the most natural supply of Berberine. The plants which are related genus are commonly used as various activities. The Berberine fruit (Berberine vulgaris) is used as blood purifying agent from the past years. Use of stem, root, bark of plant rich in Berberine. Berberis species history has quite 3000 years.

### EXTRATION METHOD

(Marek, R. et al., 2003; Grycova, L. et al., 2007) they reported that the Berberine are protoberberine alkaloid salts and they are changed in specific types of bases and extract further extracted in organic solvents. Berberine using classical extraction used different solvents e.g. acidified, aqueous mixtures, chloroform, ethanol and methanol. Sefivity was major challenged for Berberine extraction and degrade Berberine light and also in case high temperature. 13-14

(Babu, N.H.R. et al., 2012) they reported that they represent extraction process and drying temperature sample serious factor. Berberine found plant part of stem from Coscinium fenestratum and collect sample for the Berberine and extract yield from tissue sample was dried different types:

(i) Cold extraction method: in this method sample dried under refrigerator conditions (-20°C) with methanol and ethanol. 15

(ii) Hot extraction method: in this method sample dried in water bath (50°C) with ethanol and methanol.

Extract centrifuged and dried at constantly room temperature and filtered berberine sample analyzed. 15

(Teng, H. et al.2013; Choi, Y. et al. 2013) they reported that the serious stage choice of solvents considered in Berberine. The solvents used mostly for the extraction process aqueous, acidified, methanol, ethanol and alkaloid rhizomes of cycis chinensis content Berberine extract. The acidified solvents (hydrochloride acid, phosphoric acid, nitric acid, sulfuric acid and acetic acid) used with combination higher solubility with free alkaloid base salts and concentration 0.34% phosphoric acid compared with classical extraction techniques. The extraction by the reflux and soxhlet method of Berberine at higher amount of yield contain by cold acid extraction. 15

(Mokgadi, J. et al., 2013; Rojsanga, P.et al., 2005; Gritsanapan, W.et al., 2005) they reported that drawbacks of conventional methods and longtime extraction with large amount of solvents. They used maceration process procedure for the part of plant Coscinium fenestratum with total 3200ml ethanol solvent (80%) long time period. 17-18

(Rojsganga, P.et al., 2006; Gritsanapan, W.et al., 2006) they reported that the used different extraction classical extraction as soxhlet, percolation and maceration techniques. The Berberine contain from stem part of plant Coscinium fenestratum lower amount as compared to previous study. The extract material used 30g and solvents used 2000ml amount for maceration process, 600ml amount used for soxhlet extraction and 5000ml amount used for percolation extraction process. The extraction continued 7 days long time periods for the process maceration and soxhlet extraction process working 3 days. 19

(Shigwan, H.et al., 2013) they reported that a large amount solvent was used in conventional hot extraction methods. The Berberine obtained stem bark from Berberis aristata and Berberis tinctoria was used 900g with 2500ml methanol in temperature 50°C for 3 hr. The extraction method widely used traditional method to extract out of Berberine and variety method used for development. To improvement efficiency of extraction, decreased time consumed for extraction and amount of solvents used within extraction. Better results by used different extraction techniques found successfully. These methods are alternative techniques (MAE, PLE, SFE, UPE and USE) with compared with method of classical extraction. 20

(Alupului, A.et al., 2009) they reported that ultrasonically extraction and microwave-assisted extraction was considered in efficient, simple method, and cheap cost techniques. 21

(Chang, Y.et al., 2013) that was performed in lesser extraction time. In his procedure were used to selected combination ionic liquid, green solvents solutions and the extract Cycis chinensis contain Berberine by using USE method technique. 22

(Xu, K.et al., 2018) they reported that the compared many extraction methods such as soxhlet extraction and distillation extraction collect phellodendron to establish in proper manner high efficient method. The extraction of phellodendron fresh bark from Cortex phellodendri contains

### Table 3: Berberine species uses in intestinal and skin disorder

| Berberine species | References (work done) | Berberine used in intestinal disorders | Berberine used in skin disorders |
|-------------------|------------------------|---------------------------------------|----------------------------------|
| In the Berberidaceae family, they used as raw material and an important ingredient used in Ayurvedic traditional medicine and Chinese medicine. Berberis genus includes 450-500 species which represent the most natural supply of Berberine. The plants which are related genus are commonly used as various activities. The Berberine fruit (Berberine vulgaris) is used as blood purifying agent from the past years. Use of stem, root, bark of plant rich in Berberine. Berberis species history has quite 3000 years. | (Karimov, A. et al., 1993; ; Birdsaill, T.C. et al., 1997; Gupta, A. et al., 2014; Tandon, R. et al., 2004 Singh, A. et al., 2010; Amritpal, S. et al., 2010; Kullaran, S.K. et al., 2009) | Treat hepatitis A, hepatitis B, hepatitis C and hepatitis D, prostate cancer, syphilis, poliomyelitis, conjunctivitis, leishmaniasis, blood vomiting, jaundice, rheumatism, body pains, sleeping sickness, treated infectious disease such as urinary tract infection, HIV sexual asthma, diabetes, hypertension, hemostatic, intestinal spasms, intestinal worms, fatigue, constipation, dysentery, ulcer, intercostals pain, spleen in children, sore, Treat various fevers: yellow fever, rickettsia fever, typhoid fever, chills, antipyretic, malaria, Tuberculosis, coughs. | In inflammation condition, infectious disorder on skin, anti-diabetes, aches, wounds, skin ailments. |
Berberine extract. In his case, Berberinein combination of solvents used methanol, ethanol, acidified solvents and water with the extraction contain higher amount of extraction yield. They was determined that Berberine extract use of hydrochloride acidified acid, methanol and USE technique much more efficient. They concluded that the higher yield extraction compared with soxhlet method and distillation method of Berberine.

(Xi, et al., 2017) they reported that the classical extracted method technique was considered. This technique present many advantages increased the yield, extraction time reduce, quality enhanced and reduced solvent consumption.

(Guoping, L. et al., 2012) they reported that the Cortex phellodendri made comparison with different extraction techniques: heat reflux, MAE, UPE and USE techniques. The yield was obtained by extraction method in case UPE with lower extraction time and higher extraction time. Reflux, MAE and USE with 5.35mg/g for 2 hrs, 5.61mg/g for 1 hrs and 6mg/g for 15min.

(Mustafa, A.et al, 2011 ; Turner, C.et al, 2011) they reported that the considered both extraction method pressurized method and other method used accelerated solvent extraction. The plant extraction used as a technology for compound to pressurized liquid extraction and pressurized fluid extraction. The various methods of extraction of Berberine are listed in the Table 4.

Table 4: Various methods of extraction of Berberine from various crude drugs

| Sr. no. | Crude drug | References | Method extraction and Isolation | Method of analysis various analytical techniques |
|---------|------------|------------|--------------------------------|--------------------------------------------------|
| 1       | Argenome mexicana | (Samal, P.K. et al, 2013) | Method- Soxhlet extraction Solvents: methanol Dry the compound by evaporation and Re-solubilized the dried compound in methanol with required concentration. | Method- HPTLC Stationary Phase: silica gel (60F254) Mobile phase: Toluene: Ethyl acetate (9:3, v/v). Detection of compound at : 266 nm |
| 2       | Berberis aristata DC 1.5g and herb extract 0.1 g | (Singh, R. et al, 2010) | Method- Reflux isolation Solvents for extraction: Take 100 mL methanol on a water bath for 1 hr. Filter process- Re-isolate the crude by use of ES in 50 ml volume and repeat the procedure2 times for 30 min. Filtrates combination and concentration to 50ml Herb extracts Method- ultrasonic extraction Solvents: Methanol Volume: 10 mL approx. Sonication process and Filtration process is done. | Method- HPLC Column: Zorbax ODS II, 250 x 4.6mm (5μm) Mobile phase: potassium hydrogen phosphate buffer (pH 2.5). Detection at: 346 nm Temperature: 40°C Flow Rate: 1 ml/min Method- Herbal ultrasonic extraction process Solvents used: methanol (Volume 25ml minimum) Sonication process. |
| 3       | Berberis aristata, Berberis tinctoria | (Shigwan, H.et al, 2013) | Method: Hot extraction process Solvents Used: methanol (2.5 Litre) Time: Min. 3 hr Temperature: 50°C | Method- HPLC Column: Unisphere is used (C18, 150 x 4.6mm or 5μm) Mobile Phase: 0.1% (trifluoroacetic acid) Acetonitrile in the ratio of (60:40v/v) Detection at: 350 nm Temperature: 30°C Flow Rate: 1 ml/min |
| 4       | Coptis chinensis | (Teng, H, Choi, Y.et al, 2013) | Method- Acid assisted extraction process. | Method- HPLC Column used: X Terra (C18, 250 x 4.6mm) |
| 5 | **Cortex phellodendri** (Guoping, L. et al., 2012)²⁵ | **Method**: Ultrahigh pressure extraction (UPE)  
**Parameters used**:  
Solvents used: ethanol  
Ratio of liquid-solid: 31.3  
Pressure of extraction: 243.30  
Time: 2 min | **Method**: HPLC  
**Column Used**: Hypersil Oxidative Desulfurization (C18, 250 × 4.6mm and 5μm)  
**Mobile Phases used**: triethanolamine  
Solution pH: 3.5  
Detection at: 265 nm  
Temperature: 30°C  
Flow Rate: 1 ml/min |
| 6 | **Coptis rhizome** (Liu, B. et al., 2006)²⁹ | **Method**: Supercritical fluid extraction process  
Time: More than 3 hr  
Temperature: 60°C  
Pressure range: 200-500 bar  
Flow-rate of CO₂: 1 Litre/min  
Flow-rate of modifier system: 0.4 mL/min.  
Organic solvent: ethanol  
Carbon dioxide, methanol | **Method**: HPLC  
**Column Used**: Diamonsil (C18, 250 × 4.6mm and 5μm)  
**Mobile Phases used**: Potassium di-hydrogen phosphate : Acetonitrile  
Detection at: 345 nm  
Flow rate: 1 ml/min |
| 7 | *Cortex pellodendri Amurensis* | (Liu, S. et al., 2013)³⁰ | Tween  
Soxhlet extraction:  
Extraction Solvents: hydrochloric acid: methanol (1: 100, v/v)  
Time: 8 h | Method: HPLC  
Column used: Daisopak (SP-120-5-ODS_BP, 250 × 4.6mm and 5μm)  
Mobile Phases used:  
Acetonitrile  
phosphoric acid  
water ratio: [0.7:100 v/v]  
Detection at: 345 nm  
Temperature: 25°C  
Flow Rate: 1 mL/min |
|---|---|---|---|---|
| 8 | *Coscinium fenestratum* | (Rojganga, P. et al., 2005; Gritsanapan, W. et al., 2005)³⁰ | Cortex  
Method: Ultrahigh pressure extraction  
Solvents used: ethanol  
Ratio of liquid-solid : 30: 1  
Extracting pressure : 400 MPa  
Time: 4min  
Temperature : 40°C  
Method: Ultrasonic extraction process  
Solvents used: ethanol  
Soaking time for sample: 24 hr  
Sonication time: 60 min  
Temperature: 30°C  
Method- Heat reflux extraction process  
Solvent used: ethanol  
Soaking time for sample: 24 hr  
Extraction time: 4 hr  
Method- Soxhlet extraction process  
Solvent used: ethanol  
Soaking time: 4 hr  
Time of sample isolation: 4 hr | Method: TLC  
Stationary phase used: Silica gel (GF254)  
Mobile phase used:  
ethyl acetate: butanol: formic acid :water (50:30:12:10)  
Detection at: 366 nm |
| 9 | *Coscinium fenestratum* | (Arawwawala, L.D. et al., 2012; Wickramaar, W.A. et al., 2012)³¹ | Cortex  
Solvent used: methanol  
Extraction (Hot): sample refluxed with solvent upto3 hr  
Filtration: Methanol  
Evaporation: Methanol.  
Extracts Re-solubilized in: Methanol  
Method: Cold extraction process  
Solvent used: ES  
Time: 24 hr  
Filtration/evaporation | Method: TLC  
Adsorbent used: Silica Gel (GF-254)  
Solvent used: n-Butanol: Ethyl acetate: Acetic acid  
Ratio: (2.5:1.5:1, v/v/v)  
Detection at: 254 and 366 nm |
| Step | Description | Method | Parameters | Detection |
|------|-------------|--------|------------|-----------|
| 10   | Dried powder stem *Coscinium fenestratum* | Solvents used: water/methanol/water (1:1:1 v/v) | Methanol Sonication time: 15 min Temperature: room temp. Centrifugation process: 2800 rpm for 15 min. Filtration/evaporation/Resolubilization: Methanol/water Ratio: 9:1 v/v | HPLC Column used: (Oxidative Desulfurization, Chromolith, RP-18e, 100 x 4.6mm) Mobile Phases used: Methanol Deionized | UV |
| 11   | Dried form *Coscinium fenestratum* | Method- Cold extraction process Temperature: 20°C Hot extraction temperature: 50°C on water bath Solvent used: ethanol Centrifugation time: 10 min Temperature: 10°C Samples | Method: HPLC Column used: (C18, 250 x 4.6mm and 5μm) Mobile Phases used: Acetonitrile Trifluoro-acetic acid Ratio (50:50, v/v) Detection at: 344 nm Flow rate: 0.8 ml/min | |
| 12   | Goldenseal, *Hydrastis canadensis* | Method: Pressurized hot water extraction process Solvent used: water Temperature: 140°C Parameters used: Pressure: 50 bars Flow rate: 1ml/min Time: 15 min | Method: HPLC (Diode Array Diode) Column used: Zorbax eclipse Plus (C18, 75 x 4.6mm and 3.5μm) Mobile phase used: Formic Acid- pH 2.7 Methanol Detection at: 242 nm Temperature: 35°C Flow rate: 1 ml/min MS Detection by: Elect spray ionization (+) Temperature of capillary: 200°C Current: 20 V Voltage of tube lens: 5V | |
| 13   | Root *Berberis aristata* DC | Method: Soxhlet extraction process Solvent used: Ethanol is used to form an extract Desolvation: hot water filtration: hot water Acidification: HCL Cool at: ice bath Cooling time: 30min Eg: overnight in a refrigerator | Method: HPTLC Stationary phase used: Pre-coated silica gel Grade: 60GF-254 Mobile phases used: n-butanol and glacial acetic acid or water Ratio: (12:3:4 v/v/v) Temperature: 33 ± 5°C Detection at: 350 nm | |
| 14   | Rabbit plasma | Mix 100 μl of sample in 3% of formic acid with Acetonitrile solvent Solvent Volume: (200 μl) Vortex time: 30 sec | Method: Liquid Chromatography- Electrospray Ionization | |
| 15 | Rat plasma | (Wang, Z. et al., 2016) | Rat tissue |
|----|------------|------------------------|------------|
|    | Method- Rat plasma process | Method: Ultra Performance Liquid Chromatography (UPLC) or Mass Spectroscopy process |
|    | Solvent used: methanol | Column used: Acquity Ethylene bridged hybrid (C18, 50 × 2.1mm and 1.7μm) |
|    | Mixing ratio: 200 μl with standard 40 μl and 560 μl solvent. | Mobile Phase used: acetonitrile |
|    | Vortex at: 20 sec | formic acid and water |
|    | Centrifugation time: 10min rpm: 12000 | Ratio: (0.1:99.9, v/v) |
|    | Filtration process: Rat tissue | Flow rate: 0.25 ml/min |
|    | Grinding process: 3 ml saline solution with 600 mg tissue | **Mass Spectroscopy detection:** |
|    | Centrifugation time: 10min rpm: 12000 | Source of detection: Electro-spray Ionization |
|    | Mixing ratio: 200 μl with standard 40 μl in 560 μl | Quantification by: different Reaction Monitoring mode |
|    | Vortex at: 20 sec |  |
|    | Centrifugation time: 10min rpm: 12000 |  |

| 16 | Rat plasma | (Xu, B. et al., 2015) |
|----|------------|----------------------|
|    | Evaporation of the 10 μl IS with working tube | Method: Liquid Chromatography |
|    | Mixing ratio: 200 μl with internal evaporated solution | Mass Spectroscopy |
|    | Vortex time: 1min | Column used: Zorbax Eclipse eXlta Dense Bonding (C18, 150 × 2.1mm and 3.5μm) |
|    | Mixing ratio: 10 μl with 1% formic acid or 200 μl acetone | Mobile Phase used: acetonitrile and water |
|    | Vortex time: 2min | Ratio: 1% |
|    | Centrifugation time: 10min, rpm: 10,000 rpm | acetic acid and 0.001 mol/L ammonium acetate |
|    | Mixing ratio: supernatant by 200 μl methanol | Flow rate: 0.2 ml/min |
|    | Vortex time: 1 min centrifugation time: 10 min | **MS detection:** |
|    | Mixing ratio: supernatant by 400 μl acetonitrile | Source: Electro-spray Ionization |
|    | Vortex time: 1 min centrifugation time: 10 min | Quantification by: Multiple Reactive Monitoring mode |
| 17 | Rat plasma | Solvent used: Methanol Mixture: 100 μl sample with internal standard of 10 μl centrifugation time: 10 min rpm: 12,000 rpm Temperature: 4°C Vortex time-1min Evaporation: nitrogen stream Resolubilization with 100 μl solvent. | Method: Ultra Performance Liquid Chromatography Mass Spectroscopy Column used: Acquity Ultra Performance Liquid Chromatography Column used: Ethylene Bridged Hybrid (C18, 1.7 μm, 50 × 2.1mm). Mobile Phase used: Acetonitrile Flow rate: 0.4 ml/min formic acid: water Ratio: (0.1:99.9 v/v) Quantification by: Multiple reactive monitoring mode MS detection: Source: Electro-spray ionization. |

| 18 | Stem bark *Mahonia manipurensis* | Method: Cold extraction process Solvent used: Methanol Quantity: 1000 mL Stirring: room temperature | Method: TLC Stationary phase used: pre-coated silica gel (GF-254). Mobile phase used: hexane ethyl acetate methanol Ratio: (56:20:5) Fraction and purification test: Dragendorf's Reagent (+ve test) Analysis of purified fraction: Mobile phase used: chloroform ethyl acetate diethyl-amine methanol ammonium hydroxide Ratio: (6:24:1.5:6:0.3) HPLC: Column used: Water-Symmetry (C18, 250 x 4.6mm and 5μm) Mobile phase used: methanol formic acid |
| 19 | *Tinospora cordifolia* | (Satija, R. et al., 2015) | Method: Microwave assisted extraction (MAE) process  
Solvent used: ethanol  
Time: 3 min  
Method: Soxhlet extraction process  
Solvent used: ethanol  
Time: 3 hr  
Filtration  
Concentration  
Maceration  
Solvents for extraction: ethanol-200ml by 7 days irregular stirring | buffer  
Ratio: (0.1% v/v)  
Detection at: 346 nm  
Flow rate: 1 ml/min  
Detection by: UV spectra at 200 to 500 nm  
MS: Electro-spray Ionization | Method: HPTLC  
Mobile phase used:  
methanol  
acetic acid  
water  
Ratio: (8: 1 v/v/v).  
Detection at: 366 nm |
|---|---|---|---|---|
| 20 | *Tinospora cordifolia*, *Tribulus Terrestris*, *Emblica officinalis* | (Joshi, H. et al., and Kanaki, N. et al., 2013) | Solvent used for extraction: chloroform  
Sample is triturated with ammonia solution  
Dry: room temperature  
Extraction time: 1 hr  
phase extraction of chloroform with 5% sulfuric acid  
Basic nature: by acid extract with sodium carbonate  
 pH: 9  
Extraction with chloroform: X3  
Evaporation temperature: 50°C  
Residue solubilized by methanol | UV absorbance at: 348 nm (wavelength) |

The extraction process is simple and involves several steps such as sample mixing and extraction solvents e.g. acetone, acetonitrile and methanol. Centrifugation after that the supernatant in nitrogen stream and the extraction of solid phase extraction (SPE) can be applied.

**ANALYTICAL TECHNIQUES**

After Berberine extraction, separation, purification and quantification use the chromatography methods. Determination of Berberine extract by using different analytic techniques such as UV-Vis spectrophotometry, High Performance Liquid Chromatography, Thin Layer Chromatography, Capillary Electrophoresis and High Performance Thin Layer Chromatography. Berberine analyzed by Liquid Chromatography-Mass Spectrophotometry, Ultra Performance Liquid Chromatography-Mass Spectrophotometry.

**UV-Vis spectrophotometry**

(Joshi, H. et al., 2013; Kanaki, N. et al., 2013), they reported that they work done by this method was considered most effective and rapid detection method from Berberine extract quantitative analysis plant extracts. Berberine concentration determined by UV technique absorption at 348nm, based on Beer-Lambert Law. Done dilution range of 2-20µg/ml Berberine samples and compounds avoided by isolation of alkaloid fraction.11

**High-performance liquid chromatography (HPLC)**

(Sasidharan, S. et al., 2011), reported that HPLC technique widely used for quantitative analysis and qualitative analysis and also used in quantification and identification. The stationary phase of C18 silica column and mobile phase used different solvents are methanol, acetonitrile and water with combination phosphate buffers. Separation and detection of Berberine compound by using isocratic gradient elution and
high sensitivity Berberine identification using UV and DAD techniques.  

**Thin layer chromatography (TLC) and high performance thin layer chromatography (HPTLC)**

(Samal, P.K et al., 2013) they reported that two techniques used usually for Berberine detection by TLC method and HPTLC method. These methods were easy and cost effective. By the HPLC method present the chance of running samples at the same time use small quantity of samples as well as mobile phases. The plant *Artemisia vulgaris* used for the identification of Berberine by using stationary phase and mobile phase. The silica gel used as stationary phase and mobile phase used with toluene and ethyl acetate solvents.  

**Mass spectrometry:**

(Xu, B.et al, 2015) they reported that considered great techniques to analyzed samples. In this method, sample analyzed fast and accurate information related to the structural compounds composition in this technique. They developed accurate and sensitive methods to Berberine determine. Samples separation optimized by using six types of reverse phase columns, two mobile phases with different solvents such as methanol-water and acetonitrile-water, additives used in different concentration: 0.1, 0.5, 1, and 2% formic acetic acid and 0.0001, 0.001, 0.01 mol/L ammonium acetate, acetic acid and formic acid. The different method was tested in specificity, linearity, lower limit of quantification, stability, accuracy and precision.  

**The potential of Berberine on their therapeutic effects**

**Immunomodulatory potential:**

Immunomodulatory effect of Berberine was established in many experimental. Berberine furnish to relieve damage in cardiac the by increasing the anti-cardiac myosin antibodies and regulate the action of some STATs or block the differentiation of Th1 cytokines and Th2 cytokines cells. This route plays main function with the pathogenesis of myocarditis. Neurologic disease characterized by autoimmune and peripheral nervous system. The useful outcome of Berberine on animal model resided in its pressure on cellular immunity and humoral immunity and the inhibition of lymphocyte proliferation (CD4) and also decrease in pro-inflammatory cytokines (IL-6 and TNF). Multiple sclerosis is a common disease of central nervous system and inflammatory processes. Berberine enhances the level of corticosteroids. We can examine the increasing level with the help of experimentally-induced colitis in rats. The benefits and the effects of Berberine may be allow and apply to the rise in level of endogenous glucocorticoid compounds with the effective and desired therapeutic action in inflammatory bowel disease.  

The various effects of Berberine are shown with their therapeutic and mechanism in Figure 2.

![Figure 2: Potential of Berberine on their therapeutic effects and their mechanisms](image-url)
Antioxidant potential:
Normal conditions body maintains balanced the antioxidant and prooxidant agents. Imbalance between pro-oxidant and antioxidant occurs high oxidative stress. Oxidative stress build several mechanisms: a production increase of reactive species, decrease enzyme levels involved in blocking actions of compounds or decrease free radical. The Berberine on peroxidation of lipids, and effect induced after chemical carcinogenesis in small animals. Berberine detects best result of antioxidant properties suitable effect on lipid peroxidation. Further, involved mechanism in antioxidant of Berberine: free oxygen removal, ROS/RNS scavenging, nitric oxide ions and reducing destructiveness of superoxide ions. Increase the antioxidant effect of endogenous substances. Highly potential antioxidant and Berberine compared with vitamin C. The oxidative stress plays a main part.

Potential on endothelium:
Berberine induces endothelial relaxation with increasing NO production from essential amino acid through activity of endothelial nitric oxide that thought of within the dilatation method. Berberine facilitates phosphorylation of endothelial nitric oxide synthase and heat shock proteins 90, that increasing NO production. Endothelial contraction by taking Berberine and it reduced the COX-2 expression. Imbalance of the COX-1 and COX-2, activity, quantitative relation ratio between vasodilator/vasoconstrictor, and prothrombotic/antithrombotic effects. Berberine shows helpful impact on TNFα/AKT/eNOS mRNA beneficial effects.

Atherosclerotic potential:
The level of blood lipid very high levels and associated with vascular wall swollen. Effect of Berberine during lipid metabolism is the significance of cholesterol low density lipoprotein receptors. Receptors stabilize by an extracellular signal regulated kinase extracellular signal regulated dependent pathway with Berberine increases the activity of low density lipoprotein receptors through INK pathway. There are two types of enzymes; Acetyl-Coenzyme A Transferase 1 and Acetyl-Coenzyme A Transferase 2 Berberine influence on lipid profile.

Hepatoprotective potential:
Berberine was established on animal study of Berberine. Berberine reduced functional hepatic tests and histological damage (cellular infiltrate inflammation and hepatocyte necrosis). The mechanism of Berberine which reduces hepatotoxicity also considered on carbon tetrachloride (CCL4) induced hepatotoxicity. Berberine used lowers nitroamine oxidative stress and inflamed liver. The Berberine decreases. Berberine prevents decrease in increase in lipid peroxidation and super peroxide dismutase activity. Reduction in COX-2, TNF-αand caused nitric oxide synthase (iNOS) levels. Decrease in transaminase levels maintain. Berberine helps to maintain integrity of hepatocellular membrane.

Potential on glucose metabolism:
Berberine low blood sugar level, and its mechanisms Inhibition mitochondrial glucose oxidation, Incentive of glycolysis and breakdown of glucose increased and decreased ATP level through inhibition of mitochondrial function in liver and gluconeogenesis. By the Berberine inhibition of dipeptidyl peptidase-4 (DPP4), protease responsible for certain peptides such as glucagon-like peptide-1, gastric inhibitory polypeptide; rise insulin level of hyperglycemia, DPP4 inhibition. Determine peptides duration action, so improving glucose tolerance. Berberine improves the insulin resistance, and showed beneficial effects. Hypoglycemic drugs are commonly used and utilization of glucose levels in tissues with helps lowering plasma lipid free fatty acids.

CONCLUSION
Herbals are the best for the used for the treatment of various diseases with lesser side effects as compared to other formulation. In this review, we came to know about the potential uses of Berberine in the various disorders and in the treatment of various diseases. With the literature, we came to know about that extraction, isolation and analysis of this plant can be easy and can be done. So we can prepare the various formulations as herbal formulations for the treatment of various disorders in future.

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