ORIGINAL ARTICLE

Novel Application of Solubilizing Properties of Solids (Mixed Solvency Concept) for Extraction of Active Constituents from Herbal Drug Powder and Formulation and Evaluation of Topical Oily Solution of Curcumin Extract

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Abstract

Background: Since the beginning of time, humankind has employed herbal and medicinal plants as a source of food and medicine. Plant bioactive chemicals are currently of great research interest. However, extracting them as part of phytochemical and/or biological studies brings unique problems. Many techniques for the extraction of bioactive components have been devised by herbalists or scientists to indemnify the effectiveness and efficacy of the raw medications used to treat illness. The mode of extraction of active phytochemicals is receiving a lot of attention to reduce the costs associated with synthesis and separation. As a result, the extraction of active compounds from plants requires a proper procedure for extraction and techniques that provide extracts and fractions high in bioactive components, and also the solvents used in extraction do not harm humans as well as nature. As a result, they have a significant impact on yield, the nature of phytochemical content, and so on. **Objectives:** The purpose of this paper is to discuss and describe that solvents for extraction which shall be ecofriendly, safe, and also can be recovered easily by evaporation and preparation of the formulation using blends derived by idea of mixed solvency concept. **Materials and Methods:** Before extraction and formulation purity, tests were done on turmeric powder. Then, extraction was done using solvents prepared using mixed solvency such as camphor in ethanol (25% w/v and 50% w/v) and thymol in ethanol (25% w/v and 50% w/v). In addition, identification tests were done on the obtained extract. The comparative study was done on extraction yields, to establish a comparison between the yield obtained using conventional solvent and solvents prepared using the mixed solvency concept. In addition to that, a topical formulation was also prepared for the obtained extract. For formulation development solubility, studies of turmeric extract were done in various oils, ethanol, and blends (constituted in ethyl oleate with the combination of additives such as methyl paraben, propyl paraben, glyceryl monostearate, benzyl benzoate, and benzoic acid). The formulation so formed was a 0.9% curcumin oily solution and the evaluation tests such as viscosity, drug excipients interaction studies, and *in vitro* release studies were also done for the same. **Results:** In the extraction, it was discovered that adding camphor and thymol to ethanol improves the yield of turmeric extract, as compared to ethanol. Solubility studies were done for the preparation of topical solution and topical emulgel. The maximum solubility of turmeric extract was perceived in an oily blend which was formed by the purport of the mixed solvency concept). As a result, the oil base chosen for the formulation was an oily blend rather than a single oil or ethanol. In which the formulation produced positive outcomes. Evaluation studies such as freeze thaw, *in vitro* drug release, and antibacterial activity were performed for the formulation and it showed virtuous results.

Key words: Extraction, herbal drugs, mixed solvency concept, solvent systems, topical solution

INTRODUCTION

Plants are becoming more and more popular as sources of medication worldwide due to its natural origin, accessibility in local communities, affordability, ease of administration, and maybe less bothersome nature. In addition, herbal remedies might be a

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helpful alternative to conventional therapy in cases of severe side effects and drug resistance.[1]

In the standard extraction procedure, the medicinally active portion of plants or animal tissues is separated from the inactive or inert components using selective solvents. Marc is the residue left over after extracting the desired constituent, and menstruum is the solvent used in the extraction process. The impure liquids, semisolids, or powders that are produced as a result of the extractions are solely meant for external or oral use.

In the study of medicinal plants, extraction is one of the crucial steps since it is necessary to separate out and analyse the required constituent from plant material. The fundamental technique involves various steps for the extraction such as pre-washing, drying of plant materials, creating a homogeneous sample through grinding, and utilizing analytic extraction kinetics along with increasing the surface contact of the sample with a solvent solution. Appropriate precautions must be taken to ensure that any potentially active components are not lost, altered, or destroyed during the extraction of plant materials.[2]

Green extraction

Extraction techniques that require minimum energy and concede the use of quo solvents. Three key strategies have been found to design and demonstrate green extraction on a laboratory and commercial scale, as well as to approach an ideal consumption of raw materials, solvents, and energy: (A) improving and optimizing existing processes; (B) using non-dedicated equipment; and (C) improvements in techniques and procedures, as well as the discovery of alternate solvents.[3,4]

The list of the "six principles of green extraction of natural products" could serve as a guide for developing an environmentally friendly label, and standard, as well as a reminder, to innovate in all aspects of solid-liquid extraction:

- P-1: Modernity through the utilization of renewable plant resources and variety selection
- P-2: Use of alternate solvents
- P-3: Use energy recovery and cutting-edge technologies to lower energy consumption
- P-4: The industry of bio- and agro-refining should produce coproducts rather than trash
- P-5: Favor safe, reliable, and controlled processes above unit operations
- P-6: Impurity-free and biodegradable extract.

Medicinal plants

When a plant is referred to as "medicinal," it means that it contains a compound or combination of components that positively modulate the physiology of ill mammals and have been employed by man for therapeutic purposes. The terminology "medicinal plant" refers to several different plant species utilized in herbalism ("herbology" or "herbal medicine"). It involves both the study of and the use of plants for therapeutic purposes.

The Latin word "herba" and the ancient French word "herbe" are the origins of the term "herb." Tox, the term "herb" is used to describe any component of the plant, including the fruit, seed, stem, bark, flower, leaf, stigma, or root of a non-woody plant. Before, only non-woody plants, such as those that derive from trees and bushes, were referred to as "herbs."[5,6]

Turmeric: Turmeric, commonly known as *Curcuma longa*, is a native of South Asia, Indonesia, and India. The physiologically active natural polyphenol curcumin [1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-Dione], also known as diferuloylmethane, is obtained from the rhizome of *C. longa* (*Zingiberaceae* family).[7]

Mixed solvency concept[8-11]

Any weak solvent (for a specific solute) can be made strong by choosing the right solubilizing agent. For instance, oil-soluble excipients such as polyvinylpyrrolidone (PVP), vanillin, butylated hydroxyanisole, butylated hydroxytoluene, propyl gallate, benzoic acid, methylparaben, and propylparaben, when used in the right concentrations, can improve the oil solubility. Toxicology issues can be resolved by combining such excipients (solubilizers) in appropriate amounts (in comparison to the large concentration of a single solubilizing agent).

Extraction using mixed solvency concept[12]

By choosing the right solubilizing agent, any weak solvent (for a specific solute) can be made strong. For instance, using oil-soluble excipients such as PVP, vanillin, butylated hydroxyl anisole, butylated hydroxyl toluene, propyl gallate, benzoic acid, methyl paraben, and propyl paraben in the right concentrations can improve an oil-insoluble drug. The toxicity concern is resolved by combining these excipients (solubilizers) in safe concentrations (in comparison to the large concentration of a single solubilizing agent). Similarly, using the appropriate amounts of propylene glycol soluble excipients, propylene glycol-based solutions of propylene glycol insoluble drugs can be created (e.g., benzoic acid, niacinamide, sodium benzoate, PVP, and methyl paraben).

For example: Thymol (melting point around 50°C) and menthol (melting point around 45°C), two substances with differing solubilizing properties, and incorporated in powdered sesame seeds to extract sesame oil. It was found that sesame oil's solubility in melted thymol and melted menthol was excellent. Hence, in sesame oil's extraction, they were utilized. For sesame oil, ethanol proved to be a poor solvent. Moreover, sesame oil's solubility in ethanol

was enhanced by thymol and menthol, which also aided in extraction. At roughly 80°C, thymol and menthol are easily eliminated. Organic solvents are eliminated from the extracts by employing the proper methods, such as vacuum distillation and heating. Menthol and thymol are likewise removable solids due to their evaporating characteristics. They can also be recollected for recycling using the proper techniques.

Topical formulation

Advances in pharmaceutical technology have motivated formulation scientists to investigate alternate routes to oral/parenteral drug administration for efficient and effective drug delivery to the target location. Effective medication administration entails delivering medicines to the site of action in the shortest amount of time possible. The phrase "topical delivery system" describes a method of treating localised illnesses by applying the formulation to the skin, eyes, nose, and vagina.[13]

MATERIALS AND METHODS

Ethanol, thymol, camphor, vanillin, benzoic acid, ethyl oleate, glyceryl monostearate (GMS), benzyl benzoate, methyl paraben, and propyl paraben, Agar agar, Dextrose powder, Beef extract, Peptone, Yeast, and peptone were provided by Laboratory of Shri G.S. Institute of Technology and Science, Indore. All the excipients used were of analytical grade.

Steps involved in the extraction

Blends preparation

Different blends were made by dissolving compounds such as thymol, camphor, vanillin, and benzoic acid in ethanol in different concentrations. These blends were used as a solvent systems for the extraction of active constituents.

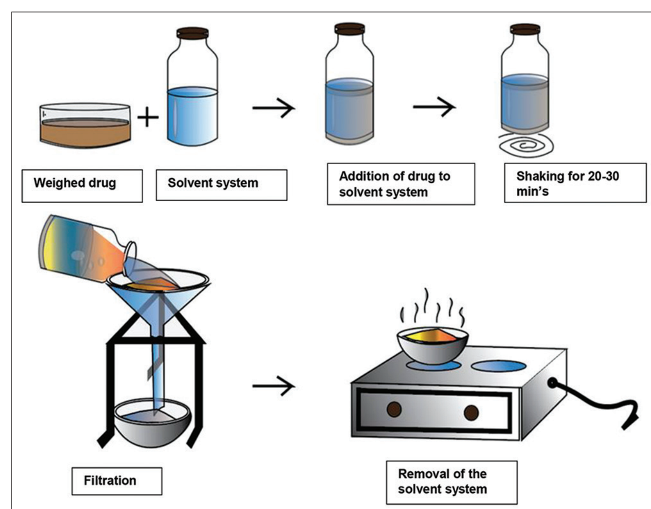

Figure 1: Procedure for extraction

Different solvent blends used were: Camphor in ethanol (25% w/v), Camphor in ethanol (50% w/v), Thymol in ethanol (25% w/v), Thymol in ethanol (50% w/v), Vanillin in ethanol (25% w/v), and Benzoic acid in ethanol (25% w/v). Ethanol alone was also used for extraction.

Extraction procedure

Each of the blends in a quantity of 5 ml was taken in vials of 10 ml capacity. To the vial, herbal drug powder (1 g) was added. After the addition of the drug powder, continuous stirring for 15–20 min was done so that each particle of the drug powder came into contact with the solvent to improve the extraction yield. When the stirring was over, the vials were kept aside for 24 h with occasional shaking. After 24 h, the filtration was done, and the filtrate was collected and transferred to the china dish as shown in Figure 1. Water bath and sand bath were used for removal of solvent systems in Table 1. Temperature condition with duration is shown in Table 1.

From Table 2, it is evident that there was better extraction using various solvent systems as compared to ethanolic extraction. Results of extraction studies of turmeric powder are reported in Table 2.

Table 1: Conditions for removal of solvent systems from the extracts

Compound	Temperature	Means used for removal of solvent system	Time
Ethanol	75–80°C	Water bath	20–30 min
Thymol	60–65°C	Water bath	30–40 min
Camphor	70–75°C	Water bath	20–35 min
Vanillin	80–85°C	Water bath	3–3.5 h
Benzoic acid	120–125°C	Sand bath	3–3.5 h

Table 2: Results of extraction of turmeric powder

Solvent	Yield		Nature of obtained extract
	In mg	In %	
Ethanol	47.00	4.70	Powder
Camphor in ethanol (25% w/v)	52.30	5.23	Powder
Camphor in ethanol (50% w/v)	46.50	4.65	Powder
Thymol in ethanol (25% w/v)	136.20	13.62	Powder
Thymol in ethanol (50% w/v)	130.70	13.07	Powder
Vanillin in ethanol (25% w/v)	189.00	18.90	Powder
Benzoic acid in ethanol (25% w/v)	146.40	14.64	Semi-solid

COMPARATIVE GRAPHICAL REPRESENTATION OF YIELD DATA

Comparison of obtained extract of different solvent systems was done to find out the effect on yield quantity of turmeric extract. The maximum yield was found in vanillin solvent system > benzoic acid solvent system > thymol solvent system > camphor solvent system > ethanol, as shown in Figure 2.

BATCH SIZE EXTRACTION OF CURCUMIN EXTRACT FROM TURMERIC

50 g of turmeric was weighed and transferred to a 250 ml volumetric flask. To the flask, 150 ml of camphor in ethanol (25% w/v) were added, and it was shaken for 25–30 min until a clear solution was obtained. The volume was made up to 250 ml using 25% w/v camphor in ethanol. And then, it was kept at the stand for 24 h with occasional shaking. After 24 h, the solution was filtered. The filtrate obtained was transferred to china dishes and kept over a hot water bath at 70–75 °C for 30–40 min to remove the solvent. An extract was obtained after the removal of the solvent. The curcumin extract was scrapped out of the china dish, weighed, and proceeded further for studies.

CHARACTERIZATION OF CURCUMIN EXTRACT OBTAINED USING 25% W/V CAMPHOR IN ETHANOL

UV spectrophotometric analysis of curcumin extract

10 mg of curcumin extract was weighed and transferred to a 100 ml volumetric flask. To this about, 70 ml of ethanol was added and the flask was shaken to get clear solution, and then, volume was made up to 100 ml using ethanol. The concentration of this resulting solution was 100 µg/ml. Then, 2 ml solution was taken and diluted up to 10 ml with ethanol. The concentration of the resulting solution was 20 µg/ml and the sample was scanned between 400 and 600 nm on a double beam UV/visible spectrophotometer (Shimadzu 1700). The maximum absorbance was found at 425 nm, as shown in Figure 3. Curcumin pure drug also shows peak at 425 nm in ethanol (as reported in literature).

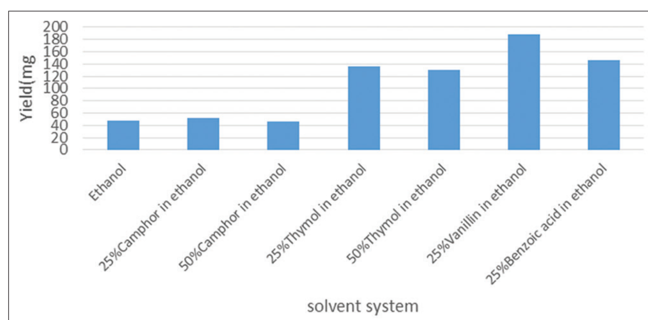

Figure 2: Extraction studies on turmeric powder

Infrared spectroscopy of curcumin

Curcumin drug powder was weighed along with the kBr. And then, the IR spectrum for the drug was recorded in the wave number region of range of 400–4000cm^{-1} on IR spectrophotometer and presented, as shown in Figure 4. The interpretation of the obtained spectrum band are given in Table 3.

Powder on fluorescence analysis

Curcumin identification was done by fluorescence analysis. Small amount of curcumin powder was taken and 1–2 drops of chemical, as given in Table 4, was added to the curcumin. Then, observation was done under visible, short UV, and long UV waves.

CALIBRATION CURVE

Preparation of calibration curve in ethanol

20 mg of curcumin extract was weighed and taken in a 100 ml volumetric flask. To this about, 70 ml of ethanol and phosphate buffer 5.5 in ration 1:1 were added and shaken to get a clear solution, and then, volume was made up to the 100 ml mark using ethanol: phosphate buffer 5.5 in 1:1 ratio.

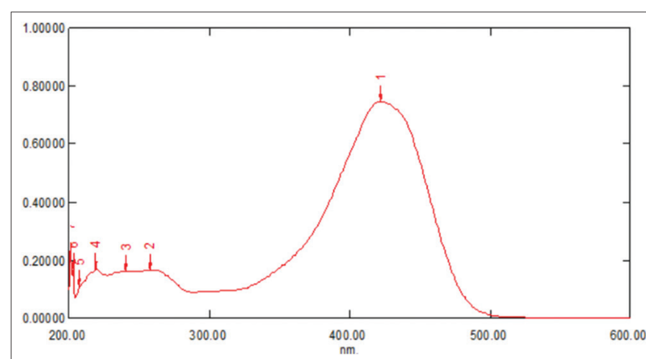

Figure 3: UV Spectrophotometry of obtained curcumin

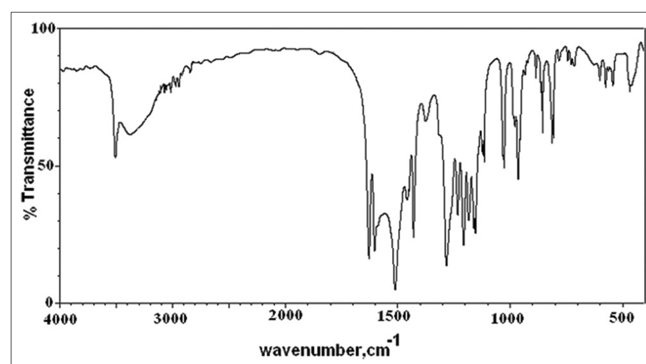

Figure 4: Infrared spectroscopy of curcumin

The resulting solution is of 200 µg/ml. From the resulting stock solution, different concentration solutions of 2, 4, 6, 8, and 10 µg/ml were prepared and their absorbances were measured in UV spectrophotometer at 425 nm as shown in Tables 5 and 6. The calibration curve was plotted between the observed absorbance and concentration as shown in Figure 5.

Drug excipient UV interference study

Before moving further for preparation of any formulation, the excipients/additives added in the blends were checked if they showed any interference with the drug.

1 g of curcumin was weighed and transferred to a 100 ml of volumetric flask, and then, volume was made up to the mark using ethanol. The resulted stock solution is of 10,000 µg/ml. From this solution, 10 ml was taken and diluted up to 100 ml using ethanol in 100 ml volumetric flask. The solution so formed is of 100 µg/ml concentration, 1 ml from this solution was taken in a volumetric flask of 10 ml and, then, diluted using ethanol for the preparation of 10 µg/ml w/v curcumin solution in ethanol. Likewise, solution of an ethyl oleate in conc. of 1000 µg/ml was made in ethanol. After preparation of solutions, absorbance of 10 µg/ml w/v of curcumin in ethanol was checked in UV spectrophotometer at 425 nm.

Absorbance of 10 µg/ml w/v of curcumin in ethanol was checked. Then, 10 ml of 10 µg/ml w/v of curcumin solution and 10 ml of 1000 ug/ml w/v ethyl oleate in ethanol solution was added to a volumetric flask of 100 ml, and then, the volume was made up to 100 ml using ethanol. An absorbance of this solution was checked in UV spectrophotometer at 425 nm to see if ethyl oleate shows any interaction with curcumin. Similarly, other additives interaction were also seen. Only in case of propyl paraben the ethanol was slightly warmed for dissolving it in ethanol. The absorbance observed at 425nm of curcumin and curcumin with excipients are given in Table 7.

After seeing the absorbance of drug and drug excipients, it is was concluded that no interaction was present between drug and excipients. As the absorbance of every compound, whether a drug or excipients showed similar absorptivity at 425 nm.

Table 3: Interpretation of infrared spectrum band of curcumin

Wave number (cm^{-1})	Interpretation
3508	OH
1628	C=O ketonic
1510	C=C aliphatic
1427	CO enol
1278	C-O phenol

APPROXIMATE SOLUBILITY STUDY OF CURCUMIN

For the preparation of oil solution of curcumin, the solubility of curcumin was checked in various oil and oil blends.

After checking the solubility of curcumin in various individual oils as given in Table 8.Some oily blends were made as per mixed solvency concept to see if curcumin solubility gets

Table 4: Observation under UV of curcumin for fluorescence analysis

Drug powder+chemical	Visible	Long UV (366 nm)	Short UV (254 nm)
Curcumin Powder+HCl	Yellow	Black	Light green
Curcumin Powder+Pet Ether	Brown	Black	Green
Curcumin Powder+HNO3	Brown	Black	Green
Curcumin Powder+Acetic acid	Fluorescent yellow	Brown	Yellow
Curcumin Powder+50% H2SO4	Crimson	Black	Black
Curcumin Powder+benzene	Light yellow	Coffee brown	Yellowish green
Curcumin Powder+methanol	Fluorescent yellow	Dark brown	Yellowish green
Curcumin Powder+50% ethanol	Fluorescent yellow	Black	Yellowish green

Table 5: Absorbance data in triplicates of curcumin extract in ethanol: Phosphate buffer 5.5 in 1:1 at 425 nm

Concentration	Absorbance 1	Absorbance 2	Absorbance 3	Std. deviation
0	0	0	0	0
2	0.242	0.217	0.218	0.011557
4	0.38	0.382	0.385	0.002055
6	0.641	0.644	0.644	0.001414
8	0.86	0.862	0.862	0.000943
10	1.1	1.066	1.12	0.022291

Table 6: Absorbance data for calibration curve of curcumin extract in ethanol: phosphate buffer 5.5 in 1:1 at 425 nm

Concentration X	Absorbance Y
0	0
2	0.225
4	0.410
6	0.643
8	0.861
10	1.095

Table 7: Result of absorbance of drug and drug with excipients

Drug and excipients	Absorbance (at 425 nm)
Curcumin	1.19
Curcumin+Ethyl oleate	1.20
Curcumin+GMS	1.00
Curcumin+Methyl paraben	1.09
Curcumin+Propyl paraben	1.14
Curcumin+Benzyl benzoate	1.11

GMS: Glyceryl monostearate

Table 8: The solubility of curcumin in different oils

Oil	Solubility
Clove oil	1.4 mg/ml
Castor oil	0.2 mg/ml
Coconut oil	0.1 mg/ml
Peppermint oil	15.9 mg/ml
Sunflower oil	1.8 mg/ml
Lemon grass oil	18.6 mg/ml
Olive oil	0.4 mg/ml
Chaulmoogra oil	2.8 mg/ml
Ethyl oleate	9 mg/ml

enhanced in oils. Moreover, it was decided that ethyl oleate will be selected as a solvent for making oily blends, because neither it showed less nor much solubility for curcumin. And also, it does not possess properties like other oils which will directly or indirectly on some instance which can affect the curcumin's property.

The blends were prepared in ethyl oleate by adding two or more components in different ratios, and then, volume was made up with ethyl oleate.

When solubility of curcumin was checked in oil blends prepared by combination of additives in ethyl oleate given in blends preparation compositions in Table 9. The curcumin showed more solubility in some blends, than some individual oils as shown in Table 10 and blends. And the blend which

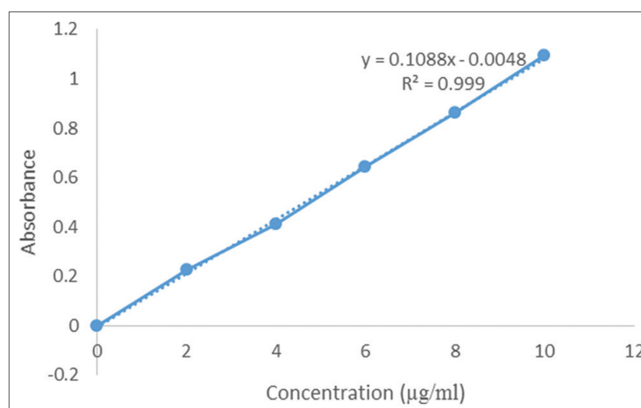

Figure 5: Calibration curve of curcumin extract in ethanol and phosphate buffer pH5.5 (1:1) at 425 nm

Figure 6: Topical solutions: Batch A and Batch B

showed maximum solubility were selected for making topical oil solution.

The blend which showed maximum solubility for curcumin was Blend 7 and Blend 3.

TOPICAL OILY SOLUTION OF CURCUMIN

Preparation of 0.9% topical oily solution of curcumin in blend 3: (Formulation-A)

Preparation of Blend 3: Methyl paraben 2.5 g, Propyl paraben 5 g, and Benzoic acid 2.5 g was weighed, and methyl pyrrolidone 2.5 ml was measured and transferred to a 50 ml volumetric flask. Then, 20 ml of ethyl oleate was added to the volumetric flask and slightly heated on a water bath at 50–60°C for 10 min. Then, volume was made up to 50 ml with ethyl oleate. The blend was prepared 50 ml. Then, topical oily solution was transferred to a container.

10 ml of the above prepared blend was taken in a 25 ml of volumetric flask and 225 mg curcumin was added to it. Then, to dissolve curcumin in the blend, continuous stirring was done and slight heating was done on a water bath at 50–60°C for 10 min until a clear solution formed, and the volume was made up to 25 ml using blend 3. Then, topical oily solution was transferred to a container.

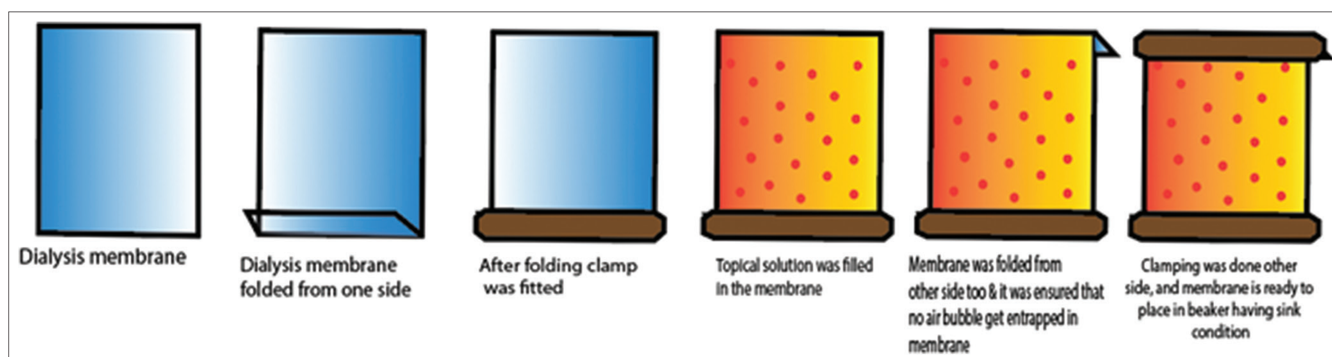

Figure 7: Drug filling procedure inside dialysis membrane for *in vitro* studies

Preparation of 0.9% topical oil solution of curcumin in blend 7: (Formulation-B)

Preparation of Blend 7-Methyl paraben 1.25 g, Propyl paraben 2.5 g, and GMS 2.5 g was weighed. Furthermore, Benzyl benzoate 10 ml and Methyl pyrrolidone 10 ml were measured and transferred to 50 ml volumetric flask. Then, 20 ml of ethyl oleate was added to the volumetric flask and slight heating was done on a water bath at 50–60°C for 10 min. Then, volume was made up to 50 ml with ethyl oleate for preparation of 50 ml blend. Then, topical oily solution was transferred to a container.

10 ml of the above prepared blend was taken in a 25 ml of volumetric flask and 225 mg curcumin was added to it. Then, to dissolve curcumin in the blend, continuous stirring was done and slight heating was done on a water bath at 50–60°C for 10 min until a clear solution formed, and the volume was made up to 25 ml using blend 7. Then, topical oily solution was transferred to a container.

Evaluation tests

- Color and transparency: The obtained oil solutions were transparent and yellowish in color
- Spread ability: When applied to the skin, oil was easy to apply and leave no stain after washing
- pH: The pH of both the oil solutions were measured using cyber scan - 510 pH meter. The pH results were between 5.5 and 6
- Skin irritancy test: No irritation was felt on the skin the after application of solution
- Centrifugation: The topical oily solutions were centrifuged at 3000 rpm for 15 min. Then, solutions were observed visually for drug precipitation
- No drug precipitation was observed
- Freeze thaw study: [14] A short-term physical stability study of the solution was performed at freezing temperatures. Physical observations were made daily to determine if precipitation or other abnormal occurrences are evident. The vials were stored at 2–8°C in the refrigerator for 24 h and, then, kept at the room temperature for 24 h. An alternate cycle like this was performed, and then vials were observed for any precipitation or turbidity
- Results: There was no phase separation, precipitation, or color change observed in the study, as mentioned in Table 11.

No precipitation, crystallization, and color change were observed during the span of 14 days. The solution became slightly turbid on freezing, but while thawing the solution again became clear within 1–2 min's at room temperature.

In vitro drug release[15]

Procedure

The formulations were evaluated for drug release the through dialysis membrane. The membrane was kept in mili-Q water for 11–12 h. Then, the membrane was again washed with mili-Q water. The sulphur compounds were removed by treating the membrane with 0.3% w/v sodium sulphite solution at 80°C for 1–2 min. The membrane was then washed with hot water having a temperature of 60°C for 2 min, which was followed by acidification with 0.2% v/v H_2SO_4. Then, the membrane was rinsed with hot water to remove the acid. After this whole procedure, the membrane was used for *in vitro* drug release.

Experimental conditions

- Release medium – Ethanol: Phosphate buffer 5.5 pH (1:1)
- Release medium volume – 200 ml
- Temperature – 37°C
- Rotation – 500 rpm.

Procedure for *in vitro* drug release study

The area of the dialysis membrane was calculated by calculating its height, breadth, and width. Then, dialysis membrane was closed from one side using a clamp and from the other side 1 ml topical solution was filled in the membrane bag. After filling of the solution, it was confirmed that no air bubble get entrapped in the membrane bag and then other side of the membrane bag was also closed with clamp as shown in Figure 7. Then, the leakage was checked. The dialysis

Table 9: Preparation of oil blends

Additives	For 100 ml	For 50 ml
Preparation of blend-1		
Methyl paraben	5 g	2.5 g
Propyl paraben	10 g	5 g
Ethyl oleate volume make up	Up to 100 ml	Up to 50 ml
Preparation of blend-2		
Methyl paraben	5 g	2.5 g
Benzoic acid	5 g	2.5 g
Ethyl oleate volume make up	Up to 100 ml	Up to 50 ml
Preparation of blend-3		
Methyl paraben	5 g	2.5 g
Propyl paraben	10 g	5 g
Benzoic acid	5 g	2.5 g
Methyl pyrrolidone	5 ml	2.5 ml
Ethyl oleate volume make up	Up to 100 ml	Up to 50 ml
Preparation of blend-4		
Glyceryl monostearate	5 g	2.5 g
Propyl paraben	5 g	2.5 g
Benzoic acid	5 g	2.5 g
Methyl paraben	2.5 g	1.25 g
Methyl pyrrolidone	5 ml	2.5 ml
Ethyl oleate volume make up	up to 100 ml	up to 50 ml
Preparation of blend-5		
Glyceryl monostearate	5 g	2.5 g
Propyl paraben	5 g	2.5 g
Benzoic acid	2.5 g	1.25 g
Benzyl alcohol	5 ml	2.5 ml
Benzyl benzoate	5 ml	2.5 ml
Valine	2.5 g	1.25 g
Ethyl oleate volume make up	up to 100 ml	up to 50 ml
Preparation of blend-6		
Glyceryl monostearate	5 g	2.5 g
Propyl paraben	10 g	2.5 g
Benzoic acid	2.5 g	1.25 g
Valine	2.5 g	1.25 g
Ethyl oleate volume make up	up to 100 ml	up to 50 ml
Preparation of blend-7		
Methyl paraben	2.5 g	1.25 g
Propyl paraben	2.5 g	1.25 g
Glyceryl monostearate	2.5 g	1.25 g
Methyl pyrrolidone	10 ml	5 ml
Benzyl benzoate	10 ml	5 ml
Ethyl oleate volume make up	up to 100 ml	up to 50 ml
Preparation of blend-8		
Glyceryl monosterate	5 g	2.5 g
Propyl paraben	5 g	2.5 g
Methyl paraben	1.5 g	0.75 g
Benzoic acid	5 g	2.5 g
Valine	1.5 g	0.75 g
Poloxamer 407	1 g	0.5 g
Ethyl oleate volume make up	up to 100 ml	up to 50 ml

Table 10: Result of approximate solubility of curcumin in blends

Blend	Approximate solubility (in mg)
Blend 1	3.60
Blend 2	4.90
Blend 3	23.90
Blend 4	5.50
Blend 5	9.40
Blend 6	2.40
Blend 7	31.80
Blend 8	15.00

Table 11: Results of 14 days freeze thaw study showing observations of precipitation and phase separation

Day	Precipitation	Phase separation	Color change
D-1	×	×	×
D-2	×	×	×
D-3	×	×	×
D-4	×	×	×
D-5	×	×	×
D-6	×	×	×
D-7	×	×	×
D-8	×	×	×
D-9	×	×	×
D-10	×	×	×
D-11	×	×	×
D-12	×	×	×
D-13	×	×	×
D-14	×	×	×

× → No precipitation, phase separation, and color change

membrane bag was put into a 250 ml beaker with 200 ml of ethanol and phosphate buffer 5.5 pH mixed together in a 1:1 ratio. To keep the sink condition, the sample in the quantity of 10 ml was withdrawn after the prescribed period of time and replaced with an equal volume of ethanol and phosphate buffer 5.5 pH. Shimadzu 1700 double-beam UV spectrophotometer, operating at 425 nm, was used to evaluate the samples.

Results of *in vitro* release study of both the batches

The release of both Formulation-A and Formulation-B is mentioned in Figures 8 and 9.

Formulation-A

The drug released from formulation-A was increased per hour()as shown in figure 8.

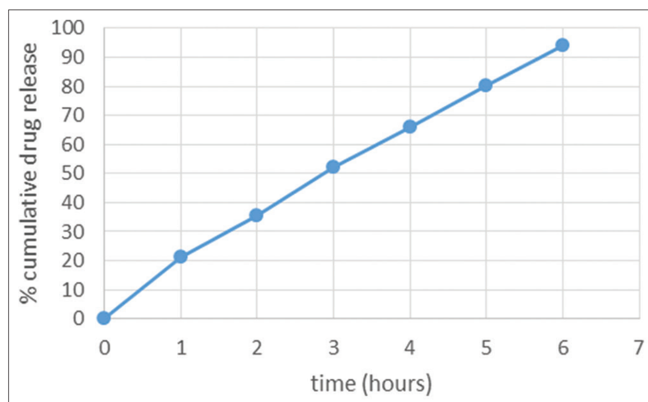

Figure 8: Graphical representation of release data of formulation-A plotted between cumulative drug release and time in hours

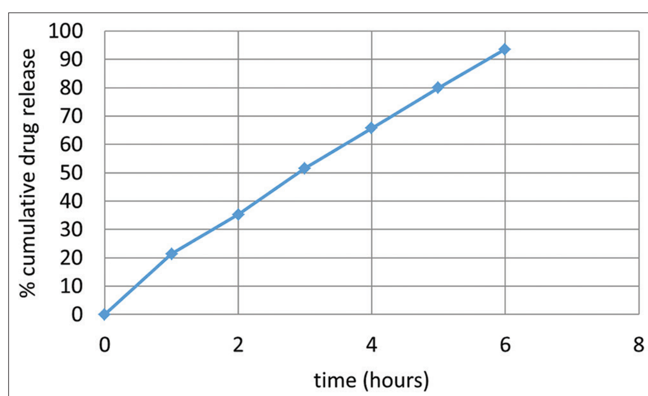

Figure 9: Graphical representation of formulation-B release data plotted between cumulative drug release and time in hours

Formulation B

The drug released from formulation-A was increased per hour()as shown in figure 9.

Antibacterial activity tests

The antibacterial activity of turmeric extract was seen on *Propionibacterum acnes*, as it was only bacteria present for the study.

MATERIAL AND METHOD

A volumetric flask of 50 mL was taken to it 20 mL of DM water which was added. Beef extract 333.3 mg, yeast 333.3 mg, peptone 500 mg, dextrose 133.3 mg, and agar 1 g were weighed. All the weighed compounds were added to the volumetric flask and stirred well with slight heating on water bath to dissolve all the ingredients, and volume was made up with water up to 50 mL. The prepared media was poured to petri dishes. After pouring the culture media to petri dishes, they were covered using another Petri dish. The Petri dishes were wrapped into a brown paper and kept in an autoclave for 15 min at 121°C at 15lb pressure.Other than Petridishes containing culture media, the 10mm paper disc were also sterilized by taking them in a petri dish and covered with another petridish. Then, wrapped using brown paper and kept in autoclave. The conditions for autoclaving were similar as mentioned above. Then, Petri dishes were taken out from autoclave. The inoculating loop was sterilized and bacteria were inoculated using that loop under UV lamp and laminar airflow chamber. After, inoculation the 10 mm paper disk was taken and topical oily solution having was applied to that and kept on the culture media surface. The Petri dishes were, then, kept for incubation. The incubation was done for 48 h. Moreover, after 48 h observation was done.

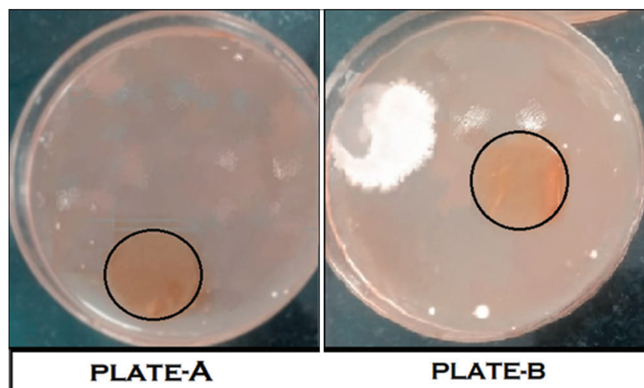

Figure 10: Plate – A showing antibacterial activity of topical solution A and Plate – B showing antibacterial activity of topical solution B

[*It was a general test performed for observing that the formulation does contain antibacterial activity. Further antibacterial studies will be done in future.*]

RESULTS

The bacterial growth was observed in white spots all over the culture media surface. However, there was no bacterial growth at the place, where disks having topical solutions were present, as shown in Figure 10.

CONCLUSION

In the prevailing study, it was found that the addition of solids such as camphor and thymol to ethanol enhances the extraction yield of some drugs as compared to ethanol. The obtained yield was then compared, and it was found that the yield obtained after each extraction of herbal drugs varied as the solvent changed, irrespective of whether the drug was similar or different. Using such solvent systems, the use of noxious organic solvents used for extraction purposes can be minimized.[16,17] Using these solvent systems, extraction yield was found to be increased as compared to the yield by use of ethanol.

In evaluation studies such as *in vitro,* the drug permeation was also similar or more than drug release studies of some of the reported formulation consisting curcumin. Here, in this research, 6 h study was done, in which both the curcumin topical oily solution showed release above 90%, while in some reported literatures, the release was about 70–80% in 24 h.[18]

This paper is based on mixed solvency concept which states that, all substances, whether liquids, gases, or solids, have the solubilizing capability. With the help of this concept, many ecofriendly blends can be made which can be used as solvents. This notion will be beneficial in both the pharmaceutical and non-pharmaceutical fields.

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CONFLICTS OF INTEREST

Author wants to affirm that there are no known conflicts of interest related to this publication or substantial financial assistance that would have impacted the 'research's findings.

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