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Formulation and Evaluation of Essential Oil-Based (Tanacetum Annuum) Nanoparticles for Rheumatoid Arthritis

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Abstract

Rheumatic arthritis constitutes severe autoimmune joint related long term inflammatory disorder that mainly affects the hand and feet joints. Approximately 1% population of the adults are suffering from rheumatic arthritis disorder. The symptoms associated with rheumatic arthritis include pain, discomfort, stiffness and swelling of different types of joints. Essential oils are naturally occurring volatile organic compounds that can be obtained from an aromatic plant. Most of them seem to have biological or medicinal behaviours that can function alone or in combination. So, they can be used in the pharmaceutical industry as a therapeutic agent. The interest in the essential oil is increasing day by day due to its vast efficacy for the treatment of several human diseases and they can possess anti-inflammatory and anti-arthritic activity. However, they are poor in water solubility, unstable in environmental conditions and most of them are impermeable across the biological membrane. Presently microemulsions are used to overcome these limitations and its pharmaceutical application. Microemulsion is thermodynamically stable in nature. Due to volatile nature of essential oil microemulsion seemed to be a better candidate for entrapment of oil. Microemulsion has advantages like it can prevent fragile compounds against enzymatic degradation, control release, improve solubilization and thus it can also improve the bioavailability of poorly bioavailable substances. The purpose of this research is to increase the solubilization, bioavailability and permeability of the essential oil for treating the disease like Rheumatic arthritis

Keywords: Dirac's elegant, Relativistic, Newtonian point

Introduction

The dimensions of nanostructured materials vary from 1 nm to 100 nm. In most cases, the surface and physicochemical qualities are a direct result of the matrix material and structure (1). There is a great deal of anticipation for it in the rapidly expanding field of modern science and technology. (2)The development of nanotechnology has resulted in improved medication delivery because of its many desirable features for therapeutic usage. The use of nanoparticles in drug delivery systems is cutting edge because it enables targeted drug administration directly to the affected area (3). There is an increase in both the pharmacokinetics and bioavailability of the drugs. Using drug-loaded nanocarriers as opposed to more conventional delivery systems may have several advantages. It helps get pharmaceuticals into cells, reduces side effects, and delays their disintegration outside and within the body (4). Medicines may be released more slowly and steadily via biological membranes, which is especially helpful for chronic illnesses. Nanoparticles are an emerging technology that has the potential to revolutionize the treatment of a broad variety of diseases and disorders via the targeted delivery of immunotherapeutic, chemotherapeutic, and biological substances (5).Therapies based on nanocarriers have helped advance biomedicine for a variety of illnesses. In the United States, the Food and Drug Administration (FDA) has either authorised several medications or is moving through the various stages of clinical testing for many

more (United-state of food and drug-administration). There is growing evidence that nanoparticle-based medicinal delivery may help reduce inflammation and arthritis (6).

Rheumatic arthritis (RA)

Rheumatoid arthritis is a long term systemic autoimmune condition that occurs quite often in women as compared to men, primarily in the elderly person. Approximately 1% of population of the adults are suffering from the rheumatoid arthritis (7). Initially, RA can affect the minor joints, progresses to major joints; ultimately it affects the skin layer, heart hair, lungs, and pair of kidneys. Joint and bone cartilage are also damaged, furthermore tendons as well as ligaments are weakened (8,9). These all-joint failure causes defects and bone destruction, which is extremely painful. Classic symptoms of rheumatic disorder involve stiffness in morning over affected area for even more than 30 minutes, nausea, fever, tiredness, weight loss, sore, swollen, and rheumatoid cysts underneath skin. Clinical revolution in the treatment of rheumatoid arthritis over the last decade — with the emergence of innovative therapeutics, the advancement of early intervention, the adoption of modern diagnostic criteria, and the implementation of new successful treatment strategies — has transformed articular and systemic outcomes.RA treatment is largely focused over the usage of DMARD (10–12). It forms in 2 main programs: csDMARD and bDMARD. Traditionally, csDMARD such as leflunomide, methotrexate, hydroxychloroquine, and sulfasalazine are often used in RA management. On the other side, bDMARD had already appeared throughout the previous 20 decades and keep on growing. It included TNF inhibitors (golimmab, infliximab, adalimumab, etanercept, and certolizumab pegol); anti b-cell, IL-6 receptor, T-cell co-stimulation inhibitor (abatacept).RA resulted in injury, inability to function, and increased mortality. Recent progress in results has been accomplished by a greater understanding of RA pathophysiology (13,14).

Scope

It is manifested that essential oil has the hopeful potential for the treatment of arthritis. Though, the low water solubility, high volatility, and instability of essential oil are major concerns and reduce its applicability in medicine. This compound seems to have a new domain and the possibility for therapeutic intervention. A microemulsion is an approach which could solve the aggravation of essential oils use via improving stability, solubility, and permeability. Microemulsion can be expected to be equivalent as micellar solutions that solubilize the oil domain in the non- surfactant tail to provide a robust microstructure. Microemulsion is being used to improve targeting of drug throughout treatment of several diseases. The formulation and evaluation of microemulsion containing essential oil was conducted in order to establish a delivery mechanism for treating rheumatic arthritis and the scope of the developing microemulsion is:

- Sustained release
- Controlled release
- Modulation of the kinetics of the drug release
- Decrease toxicity
- Enhanced drugs absorption

Formulation, Development and Evaluation

Drug profile (Essential oil)

Blue tansy oil

Synonym: Tanacetum annuum

Extraction method: Steam distillation

Odor: Sweet, herbaceous, and fruity aroma

Color and appearance: Dark blue in color

Flash point: 98ºC

Solubility: Soluble in alcohols and oils, Insoluble in water

Storage: Stored in a well-closed container away from light and moisture

Excipients profile

The excipients were used in the preparation of microemulsion was given below in Table 4.1.:

S.No.	Excipients	Profile
1.	Ethyl alcohol	Co-surfactant
2.	Tween 80	Surfactant
3.	Peanut oil	Oil
4.	Water	HPLC grade water

Table 1: The excipients used in the formulation

The methodology unfolds with an array of pre-formulation studies aimed at comprehending the essential oil's characteristics. Organoleptic properties, such as odor, color, and physical state, are assessed visually. Solubility studies explore the compound's solubility in different solvents based on their polarity. Specific gravity determination involves a bottle technique, while partition coefficient calculation is executed through a shaking flask method, providing insights into the oil's preference for different phases.

Compatibility studies are conducted to evaluate potential interactions between essential oil and excipients under varying conditions. Moving on to formulation, a pseudo-ternary phase diagram is constructed, using peanut oil, Tween 80, HPLC-grade water, and ethanol. The formulation process involves preparing a microemulsion by incorporating blue tansy oil into selected regions of oil and water phases.

The evaluation of the microemulsion formulation encompasses diverse parameters. Physical appearance, specific gravity, pH determination, viscosity assessment using a Brookfield viscometer, dynamic light scattering for particle size determination, and conductivity measurements are conducted to ascertain various attributes. Stability analysis examines the formulation's stability under different temperature conditions.

Additionally, gas chromatography-mass spectrometry (GC-MS) is employed to analyze the composition of the formulation and identify any contaminants. The comprehensive data collected is subjected to statistical analysis, employing ANOVA to assess the significance of variations.

Results and Discussion

Pre-formulation studies

Organo-leptic properties

The organo-leptic properties of blue tansy oil were evaluated by visual examination and expressed in Table 5.1:

S.No.	Parameters	Observation
1.	Color	Dark blue
2.	Odor	Sweet and fruity
3.	Physical state	Liquid

Table 2: Organo-leptic properties

Solubility studies

The study of blue tansy oil was determined by different solvents in Table 5.2:

S.No.	Solvents/Oils	Soluble/Insoluble
1.	Ethyl alcohol	Soluble
2.	Water	Insoluble
3.	n-hexane	Soluble
4.	Peanut oil	Soluble
5.	Almond oil	Insoluble
6.	Coconut oil	Soluble

Specific-Gravity

It was estimated by using bottle of specific gravity. It was calculated by:

Bottle weight, W1 = 24.12g

Bottle weight + Distilled water, W2 = 58.56g

Bottle weight + blue tansy oil, W3 = 55.12g

Mass of the blue tansy oil = W3-W1 = 55.12 - 24.12 = 31g

Mass of distilled water = W2-W1 = 58.56 – 24.12 = 34.44g

Specific gravity of blue tansy oil = Mass of blue tansy oil / mass of distilled water

= 31/34.44 = 0.9 kg/m3

Partition coefficient

The partition coefficient of blue tansy oil was calculated by using UV spectroscopy and the absorbance was expressed in Table 5.4:

Concentration (µg/ml)	Absorbance
1	0.206
2	0.423
3	0.641
4	0.834
5	0.998

Table 4: Absorbance of blue tansy oil in water

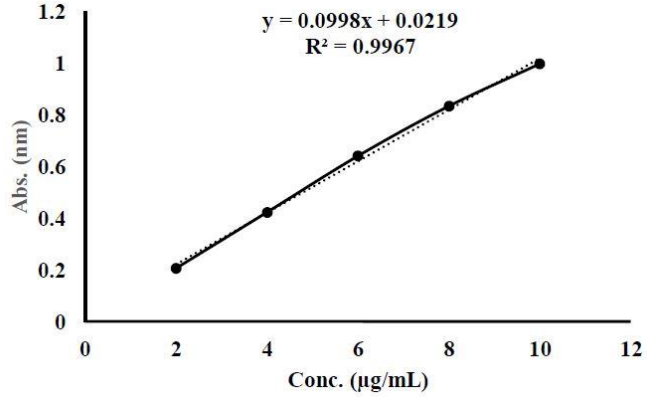

Fig. 1: The Standard curve of blue tansy in the water

Furthermore, the absorbance of the blue tansy oil in n-octanol was calculated by using UV spectroscopy as shown in Table 5.5.

Concentration (µg/ml)	Absorbance
1	0.146
2	0.254
3	0.352
4	0.453
5	0.536

Table 5: Absorbance of blue tansy oil in n-octanol

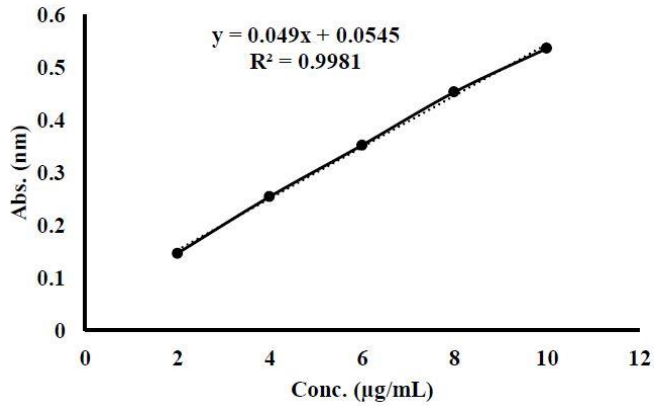

Fig. 2: The Standard curve of blue tansy oil in the n-octanol

The concentration of essential oil in both water and n-octanol was calculated by using equation:

Blue tansy oil in water

y = mx+c

0.206 = 0.0998x+0.0219

X = 1.84

Blue tansy oil in n-octanol

y = mx+c

0.146 = 0.049x+0.0545

X = 1.86

Partition coefficient = (Concentration of essential oil in organic phase)/(Concentration of essential oil in aqueous phase)

=1.861.84

= 1.01

Pseudo-ternary-phase-diagram

The pseudo-ternary-phase-diagram was made for find out the region of microemulsion. The formulation compositions were shown below in table 5.6 and 5.7.

Table 6: In this table 1:1 and 2:1 surfactant and cosurfactant percentage was given:

S-Co mix Oil

S-Co mix	Oil (%w/w)	Water (%w/w)	S-COmix (%w/w)	% Oil	% water	%S-co mix
1:2	0.1	0.9	5.4	1.56	14.06	84.37
	0.2	0.8	6.6	2.63	10.52	86.84
	0.3	0.7	8.2	3.26	7.6	89.13
	0.4	0.6	10	3.63	5.45	90.9
	0.5	0.5	12	3.84	3.84	92.3
	0.6	0.4	13	4.28	2.85	92.8
	0.7	0.3	15.3	4.29	1.84	93.86
	0.8	0.2	18.4	4.12	1.03	94.84
	0.9	0.1	20	4.28	0.47	95.23
2:1	0.1	0.1	0.1	0.1	0.1	0.1
	0.9	0.9	0.9	0.9	0.9	0.9
	4.3	4.3	4.3	4.3	4.3	4.3
	1.88	1.88	1.88	1.88	1.88	1.88
	16.9	16.9	16.9	16.9	16.9	16.9
	81.1	81.1	81.1	81.1	81.1	81.1
	0.2	0.2	0.2	0.2	0.2	0.2
	0.8	0.8	0.8	0.8	0.8	0.8
	5.4	5.4	5.4	5.4	5.4	5.4

The pseudo-ternary-phase-diagram was presented for 1:1 and 2:1 in fig 5.3 and 5.4 given below.

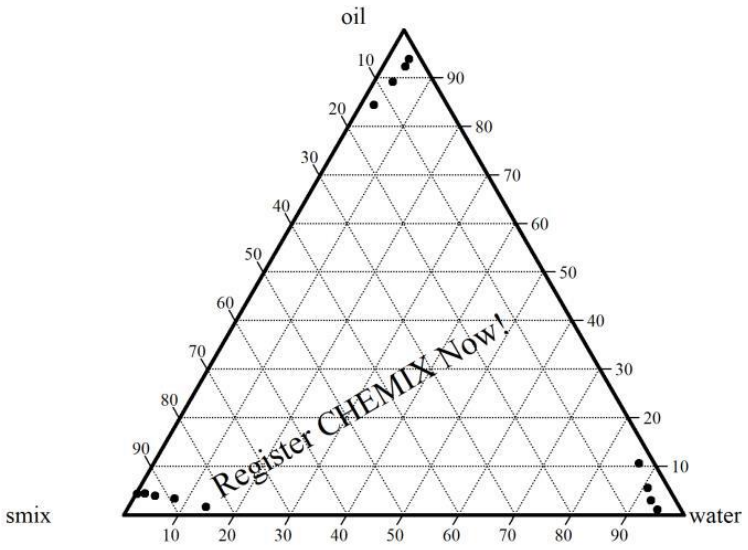

Fig 3: Pseudo ternary phase diagram of 1:1 surfactant and co-surfactant ratio

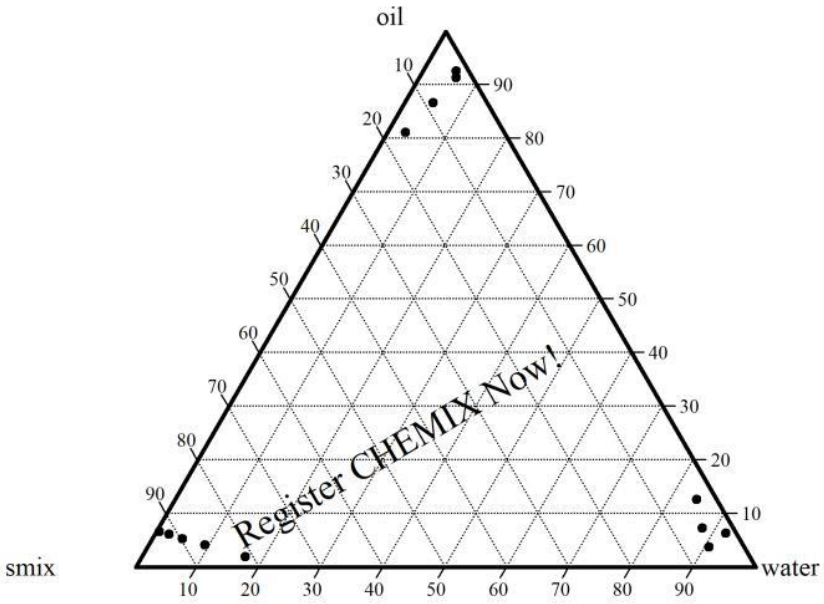

Fig 4: Pseudo-ternary-phase-diagram of 2:1 surfactant-cosurfactant ratio

SUMMARY AND CONCLUSION

Summary

In this thesis contains various sections i.e., Introduction, review of literature, scope, plan of work, material and method. The contents comprise different section summarized as follows:

The introduction section focuses on the essential oil and microemulsion and their use against Rheumatoid arthritis. It also emphasizes the importance of microemulsion in increasing the permeability and bioavailability improvement of essential oil. Different types of essential oil encapsulated nanostructures are also discussed. Patented formulations of essential oil are discussed in brief.

The review of literature section stated about the studies that were previously done by the researchers. It contains the studies associated with the formulation and development of essential oil based microemulsion. This section is very helpful regarding the selection of essential oil and excipients.

The scope of the preparation is to increase the bioavailability and permeation of essential oil. The preparation main scope is to treat the Rheumatoid arthritis.

One section contains materials and method that are used to prepare the formulation. Materials includes Blue tansy oil, Ethyl alcohol, Tween 80, Peanut oil and HPLC grade water. Method contains the pre-formulation study of the blue tansy oil which include organoleptic property, specific gravity, partition coefficient and compatibility study of the oil. The method also contains the techniques for preparing the microemulsion. The main method used in the preparation is titration method.

Conclusion

Essential oil has the hopeful potential for the treatment of Rheumatoid arthritis. Usually, essential oil has low water

solubility, high volatility, and instability. For overcome these types of limitations microemulsion is the only approach for improving solubility, stability, and permeability of the essential oil.

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