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FORMULATION OF QUININE SULPHATE MICROEMULSIFYING SUPPOSITORY FOR BETTER ENHANCEMENT.

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Abstract

Malaria, a parasitic infection, causes many voluminous illness episodes and a large number of deaths on an annual basis, nearly all of them occurring within the poorer and a lot of vulnerable sectors of the world's developing countries. Despite the enormous burden of suffering caused by malaria, the human rights implications of this ill health have not been clearly outlined. The microemulsion is prepared using a phase titration method and the suitable drug is added to the microemulsion, the resultant microemulsion with cocoa butter melt drug is poured into the suppository mould to form suppositories using the fusion moulding method. The optimized formulation of the microemulsion was prepared using the special cubic model and the microemulsion was evaluated for different physicochemical evaluation, invitro drug release, globule size, and % transmittance. Results of quinine sulphate microemulsion revealed that clear solution obtained for Microemulsion S mix ratio (1:1) oil: S mix ratio (8:2). The microemulsion ME6 shows better 98.63 % of drug release, 95.48 % of transmittance, globule size of 208 nm. The optimized formulation ME10 shows 95.146% of drug release, 97.001% of transmittance and a globule size of 219.56nm. All the formulation (MES1- MES6) micro emulsifying suppositories evaluated showed comparable dissolution & drug release results with MES4 is best, since 98.75% of drug dissolved in 30 min in dissolution studies and 90.38% of drug released in 6 hours in diffusion studies. The current study intends to develop self-microemulsifying quinine sulphate suppositories for the medication of malaria with an earlier onset of action and more lasting effect.

Keywords:

Microemulsion, Suppository, Quinine sulphate and Antimalarial

Introduction:

Since over 30% of people worldwide have parasitic illnesses, making parasitic diseases of enormous worldwide significance. Malaria is the most dangerous parasite infection, and it is responsible for 1 million to 2 million fatalities annually worldwide. Malaria is more common in tropical nations like India, where 2 million cases are reported yearly. Human malaria is brought on by four different parasite types of Plasmodium: P.vivax, P.falciparum, P.malariae, and P.ovale (1)

Microemulsifying formulations are isotropic compositions incorporating a lipid basis, a surfactant or surfactant pair, a cosurfactant or cosurfactant pair, and a medication. They are familiar to instantaneously producing fine O/W microemulsions in water with mild agitation, producing the perfect delivery system for hydrophobic medicines with sufficient oil solubility for rectal administration. Because the medication is solubilized and the generated droplets are tiny, there is a considerable interfacial surface area for drug absorption. (2)

Microemulsions are a method for enhancing the penetration of drugs that are sparingly soluble. It improves the solubilization of lipophilic medications and provides resistance against oxidation and enzymatic hydrolysis, has a long shelf life, and is simple to prepare and administer, making it a viable drug delivery system. enhance since the bioavailability. (3) The physical characteristics of the drug determine the choice of suppository bases. The drug's capacity to breakdown and diffuse through the mucus may put a cap on how quickly it reaches the rectal mucosa from the colorectal lumen. (4)

Suppositories are one of solid dosage forms which are inserted into rectum, where they will liquefy, soothe, or break down which gives localised or systemic effects. (5) Acting on medicine when experiencing nausea and vomiting orally may cause emesis, resulting in the medicine being vomited before it is absorbed. Irritation of the small intestine and stomach can be prevented from being connected with medications. when oral consumption is constrained such as before radiographic examinations, before surgery, inpatient experiencing upper GIT illnesses or when a patient is unable to swallow. It is helpful for children, the elderly, and the unconscious patient having trouble eating oral route.(6)

Currently the quinine sulphate suppositories are available, there is the need for alternative and more easily absorbed of micro emulsifying-based quinine sulphate suppositories for treatment of malaria, the oral bioavailability quinine sulphate is 76 to 88% which is difficult to children's below 5 years of age (paediatrics) accompanied with vomiting which make difficult for oral drug administration. Thus, the present investigation was to formulate micro emulsifying suppositories of quinine sulphate for treatment of malaria which is easy to use and does not required help of expert. Presently no micro emulsifying quinine sulphate suppository is available for use.

MATERIALS AND METHODS

Materials

Quinine sulphate was purchased from Yarrow chem products, Mumbai. Isopropyl myristate purchased from S-D fine chem limited, Gujarat. Span 20 gifted from Rolex chemical industries, Mumbai. Ethanol purchased from Changshu hangtag fine chemical co. ltd, Jiangsu. Cocoa butter purchased from Minimal Cocoa butter. Paraffin liquid light purchased from Bharath scientific, Bangalore

Methods

Solubility of oils, surfactant, co surfactant in Drug Quinine sulphate:

Quinine sulphate was examined with a variety of oils, such as isopropyl myristate, Flaxseed oil, Olive oil etc. Surfactant like Tween 80, Tween 20, Span 20 etc. Co-surfactants like Ethanol, Propylene glycol, Polyethylene glycol 300 etc.

Construction of Pseudo ternary phase diagram:

Using the phase titration technique, a phase diagram was created. Phase diagrams were used to construct different regions of microemulsion formation, from which many potential microemulsions could be determined. Ratios of 1:1, 1:2, 2:1, 1:0.5 pseudo ternary phase diagrams are plotted (7)

Preparation of quinine sulphate microemulsion:

The microemulsion was prepared by using the phase titration method. Different mixtures of S mix (Surfactant and Cosurfactant) i.e., Ethanol and Span20 were prepared and the weight ratios were fixed to 1:2, 1:1, 2:1, 1:0.5

.These mixtures (S/Cos) were combined with the oil phase (IPM) at the following weight ratios 9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7, 2:8, and 1:9. Water was then incorporated drop by drop, and the mixture was repeatedly stirred with a magnetic stirrer to create a homogenous dispersion or solution. The system was monitored for physicochemical characteristics following every addition. The solution cloudiest or turbid point served as the titration endpoint. It was recorded how much water phase was required to turn the combination turbid. Pseudo ternary phase diagram is counterplotted.

OPTIMIZATION: To achieve a goal, such as maximising, reducing, or targeting a responsible variable, optimization is a method of searching along process variables of input variables. The quantity of water, surfactant, cosurfactant, and oil was calculated. The objective of DOE was to accomplish desired results by optimising the crucial process parameters such as globule size, transmittance, drug release at 6 hours. D optimal quadratic design was selected to carry out with 9 experimental runs for the formulation of microemulsion. The analysis was performed actual v/s predicted and optimization were conducted in quadratic model.

Morphology (Physical appearance): For the physical appearance of microemulsion examined optically for uniformity, flexibility, and optical transparency

% Transmittance: Transmittance (%T), a measurement of transparency, was used to assess the clarity of micro-emulsions. Such values of high % transmittance (> 90%) confirmed the optical clarity / transparency of the formulation, a prerequisite for microemulsions(8)

In-vitro diffusion drug release: Franz diffusion cell with a volume of 250 mL can be taken for diffusion drug release. Completely fill the receptor compartment with buffer. The cellophane membrane with donor chamber holding the quinine sulphate microemulsion formulation. At regular intervals, samples from the receptor compartment were taken out and analysed for drug content using a UV spectrophotometer that operates at a certain wavelength.(9)

Determination of thermal stability: Samples are taken frequently for visual inspection to look for physical changes including turbidity, coalescence, and loss of clarity, among others. Additionally, the samples may be

checked to see whether there is loss of aqueous phase, which is a necessary component of the stability of the microemulsion.(10)

Preparation of Quinine sulphate suppositories using Coccabutter:

To prepare micro emulsifying suppositories using the fusion method, the cocoa butter used as the suppository base first has to be melted in a China dish. Once the mixture has cooled, it must be poured into a suppository mould while the drug-containing microemulsion is mixed in with the cocoa butter and refrigerated. The suppositories are removed from the mould once the substance has solidified.(11)

Determination of displacement value:

Prepare and measure 10 cocoa butter-containing suppositories: A gram.

Make 10 suppositories with 40% medicament and weigh them: B gram.

Determine the base content of the medicated suppository: (60/100) ×B = C gram

Determine the quantity of medication in the medicated suppository: (40/100) ×B = D gram.

Estimate the amount of base that D grams of medication shifts: (A-C) gm

DV of drug = D/ (A-C) (12)

Determination of quinine dose in micro emulsifying suppository: Quinine sulphate loading doses of 20 mg/kg parenterally should be administered to children with severe malaria, then 7.5 mg/kg every eight hours. Quinine sulphate 10 mg/kg may be administered orally every 8 hours until recovery has started.(13)

Quinine sulphate: 10mg/kg orally (Pediatric children)Half-life T½: 8 hours

Release time: 6 hours

Dt = Dn (1+KT)

[Dn- Normal dose, K=0.693/ T½, T= Time]Dt= 10 (1+ 0.0693/8 × 6)

=15.197 mg / day

Physical evaluation (Appearance): All the micro emulsifying suppositories must be equal size and form. They ought to seem sophisticated. The air in the molten mass causes individual micro-emulsifying suppositories to break and develop pits.

Uniformity of weight: Weigh each of the 10 micro-emulsifying suppositories to estimate their average weight. The average weight should not differ from more than two individual weights by more than 5%, and no weight should deviate by more than 10%.(14)

Disintegration test: The amount of the dose form that dissolves in bodily fluid in a given amount of time. It is an estimate of how quickly the micro-emulsifying suppository releases the medication.

Liquefaction time (softening): The softening period is the period before a specific temperature causes a micro emulsifying suppository to entirely melt. This test analyses the softening time of micro emulsifying suppositories, which reveals the base's hardness.(15)

Melting point Determination time: The micro emulsifying suppositories is measured by heat stability. The entire suppository must wait until a water bath with a consistent temperature to dissolve with appropriate time is taken.

In vitro dissolution studies: Release Profiles (in-vitro drug release) towards micro emulsifying quinine sulphate of 6 prepared suppositories. The results profile was measured in a pH 7.4 dissolution media. This represents the pH of the rectum. 5ml samples were pippeted from the dissolution medium at time gap of 5,10,15,20,25,30 min.(16)

Invitro diffusion studies: In vitro diffusion studies were done by Franz diffusion cell. Beaker containing 250 m of pH 7.4 & magnetic stirrer placed kept at 37±0.5°c temperature. Samples of 1 mL taken out at 1, 2, 3 ,4 ,5,6 hours time gap. (17)

Results and Discussion:

Solubility studies: Oils: Olive oil shows solubility 0.257 and 10.28%, Almond oil solubility 0.958 and 38.32%, Isopropyl myristate solubility 2.408 and 96.32%, Flaxseed oil solubility1.803 and 72.2%.

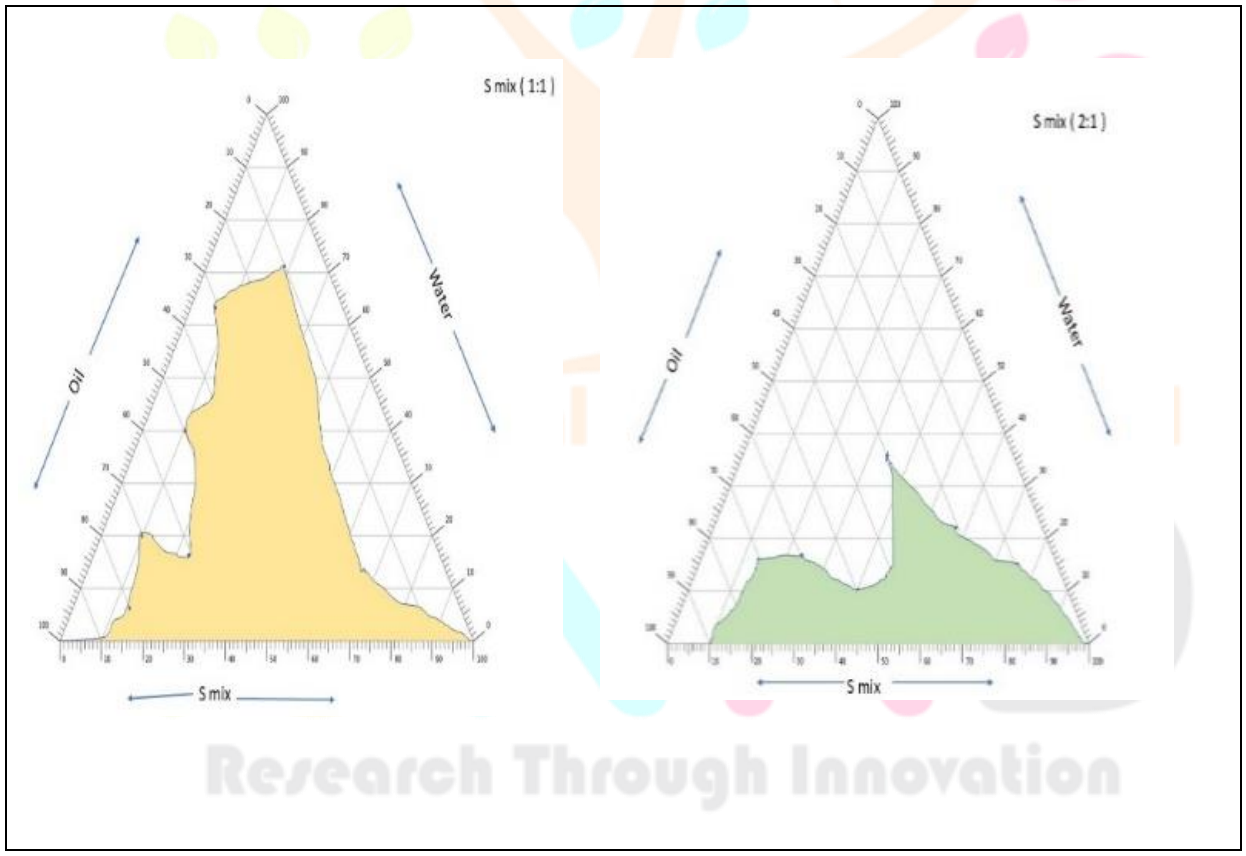
Surfactant: Propylene glycol shows solubility 0.639 and 25.56%, Ethanol solubility 1.116 and 44.64%, Polyethylene glycol 300 solubility 0.256 and 10.24%.

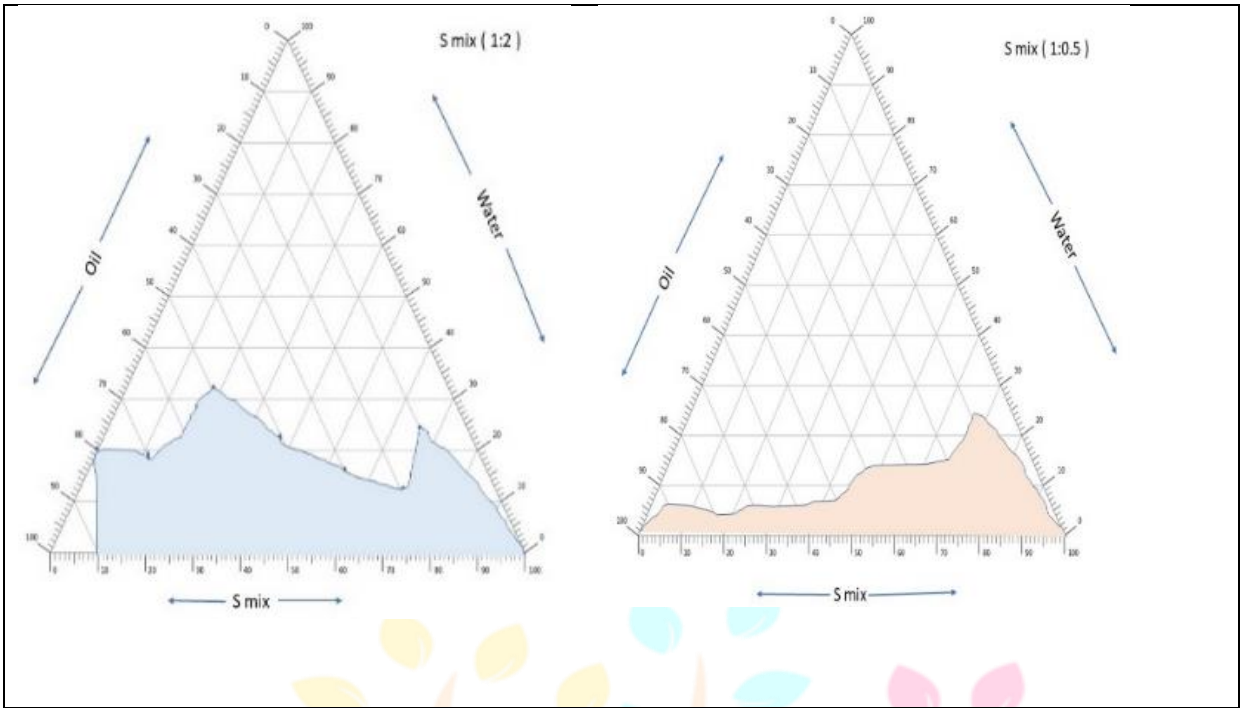
Cosurfactant: Tween 40 shows solubility 0.681 and 27.24%, Span20 solubility 2.408 and 96.32%, Span80 solubility 1.783 and 71.32%, Tween 80 solubility 2.081 and 83.24%.

Quinine sulphate shows good solubility in isopropyl myristate (oil), Ethanol (surfactant) and Span 20 (Cosurfactant).

Pseudo ternary phase diagram constructed for S mix (1:1), (2:1), (1:2) and (1:0.5)

The quaternary system of isopropyl myristate/ethanol/span20/water was used to study the microemulsion pseudo ternary phase diagram. At room temperature, the formation of the ME system is seen (shaded area). Phase experiments demonstrate that when S mix ratio is 1:1, the most ME is produced. Surfactants and Co surfactants play a significant part in ME formulations, which helps to explain this. The pseudo ternary phase diagram was drawn out using by Microsoft power point AB axis as oil, BC axis as water and CA as S mix. The obtained figure is shown

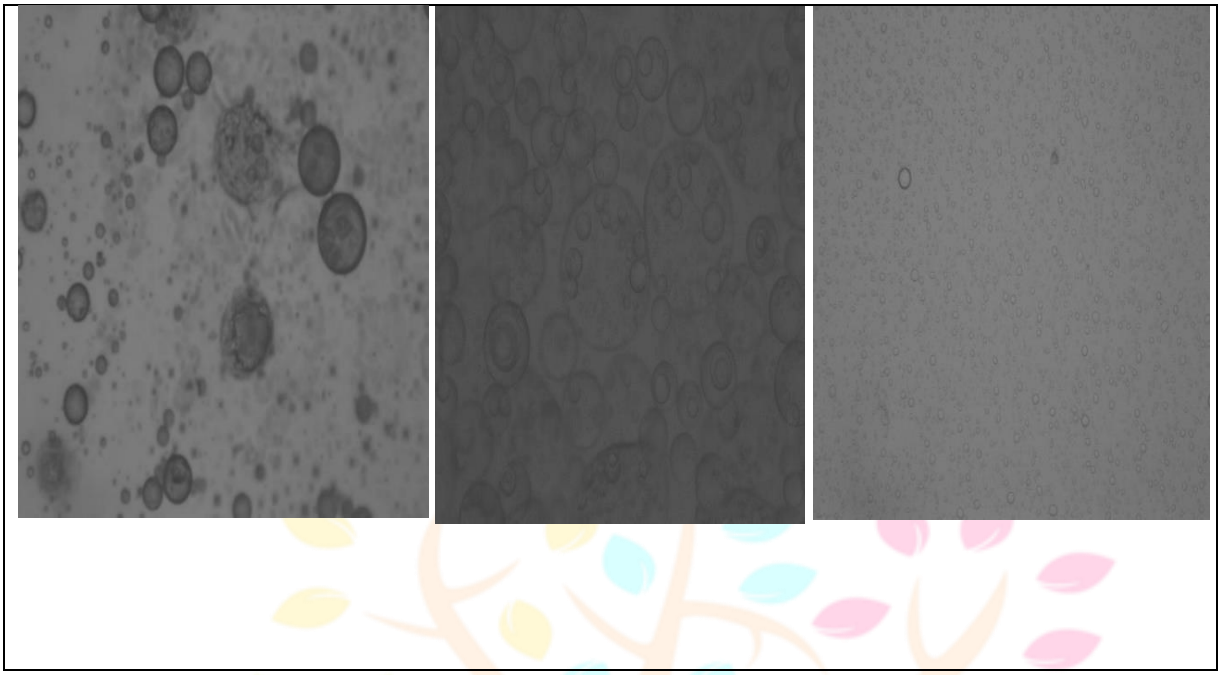




Preparation of Quinine sulphate microemulsion:

Ratios	Oil (ml)	S mix (ml)	Water (1:1) (ml)		Water (2:1) (ml)		Water (1:2) (ml)		Water (1:0.5) (ml)	
1:9	1	9	7.1	Turbid	1.7	Turbid	3.6	Turbid	2.3	Turbid
2:8	2	8	1.3	Turbid	2.1	Turbid	2.3	Turbid	1.4	Turbid
3:7	3	7	6.3	Turbid	3.6	Turbid	1.8	Turbid	1.3	Turbid
4:6	4	6	4.6	Turbid	1.3	Turbid	2.2	Turbid	1.2	Turbid
5:5	5	5	4	Turbid	1	Turbid	3.3	Turbid	0.8	Turbid
6:4	6	4	1.7	Turbid	1.6	Turbid	2.5	Turbid	0.6	Turbid
7:3	7	3	2	Turbid	1.7	Turbid	1.9	Turbid	0.6	Turbid
8:2	8	2	0.5	Clear	0.7	Turbid	2	Turbid	0.3	Turbid
9:1	9	1	3.2	Turbid	1.8	Turbid	2.7	Turbid	0.7	Turbid

Optical microscopic images of clear solution of microemulsion Smix ratio(1:1) oil:Smix (8:2) and Preparation of Quinine sulphate Microemulsion



Anova for linear model

Model Comparison: Summary statistics for Quinine sulphate microemulsions responses of R1-Globule Size, R2- Transmittance, R3 - Drug release at 6 hours

Table: An overview of the measured responses ANOVA and Regression analysis

Responses	Model	R^2	Adjusted R^2	Standard deviation	Coefficient of variation	Sum of square	Degree of freedom	Mean sum of squares	F-value	p-value	Model Significance

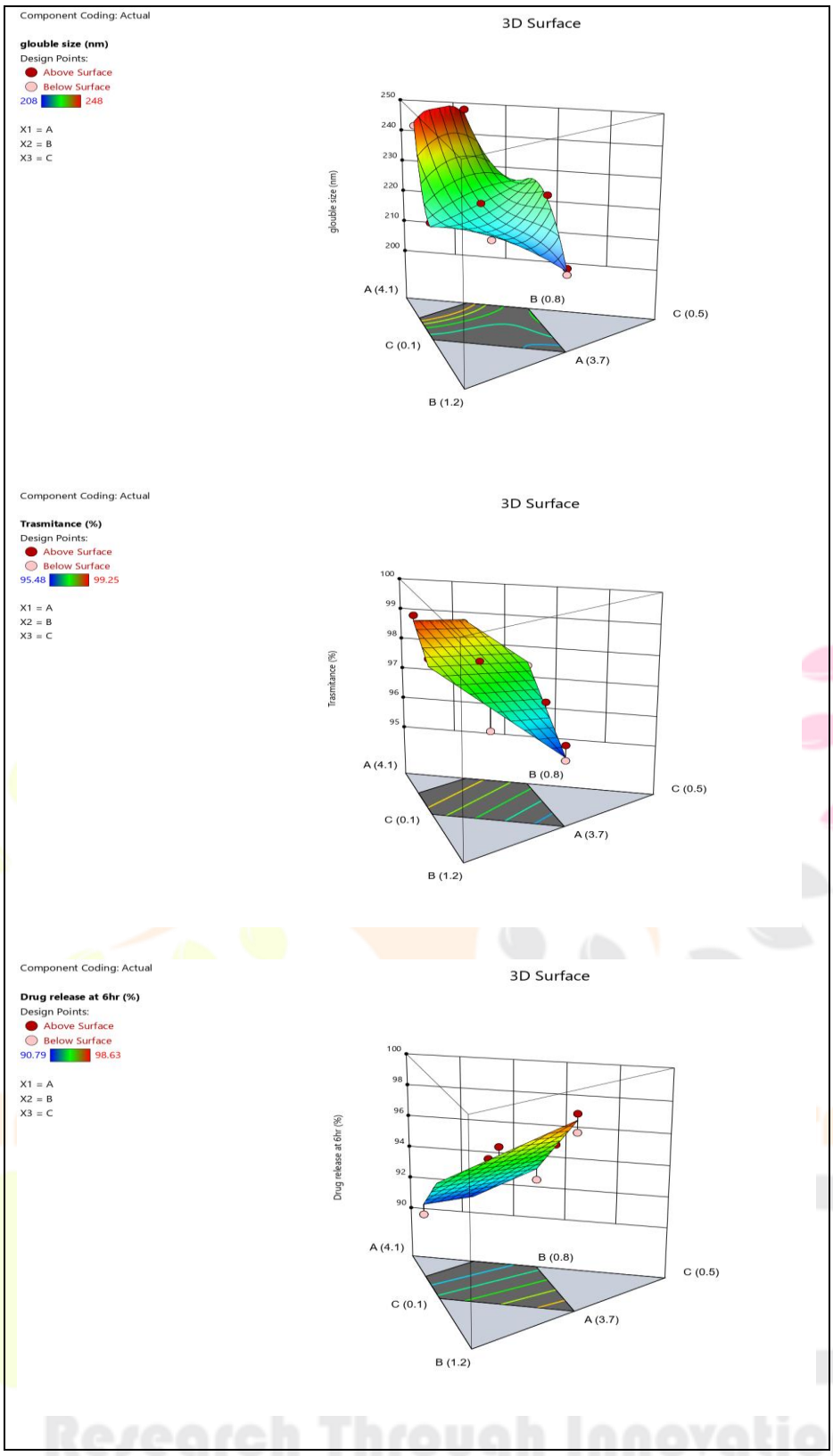
R1	Special cubic model	0.9929	0.9716	2.36	1.05	1561.7	6	260.2	46.63	0.0211	Significant
R2	Linear	0.9365	0.9154	0.3817	0.3921	12.90	2	6.45	44.27	0.0003	Significant
R3	Linear	0.9427	0.9236	0.7496	0.7924	55.48	2	27.74	49.36	0.0002	Significant

R1: Particle Size, R2: Percent Transmittance, R3: Drug release at 6 hours

Percentage composition of quinine sulphate microemulsion

Formulation code	IPM %	S-MIX %	WATER %
ME1	3.9	0.9	0.2
ME2	3.9	1	0.1
ME3	4	0.8	0.2
ME4	3.9	0.8	0.3
ME5	3.80981	1	0.190186
ME6	3.80087	0.899132	0.3
ME7	3.7	1	0.3
ME8	3.7	1	0.3
ME9	4	0.9	0.1

Response surface 3D counter graph for Globule size, % Transmittance and drug release at 6 hours



Response 1: The estimate of globule size was made using the quadratic model. The globule size model's result is significant, as indicated by the F-value of 40.63 and the p-value of 0.0211. The values AB 96.70, AC 130.80, BC 80.49, and ABC 112.61 are given for the mathematical model equation in terms of coded factors, which enables comparing the factor coefficients to assess their relative effects. The adjusted experimental globule size ME10 of 219 nm and the predicted globule size ME10 of 219.56 are reasonably in accord.

Response 2: The quadratic model was the one that was recommended as having the greatest match for the transmittance percent, a critical measure of the quality of the emulsion. The statistical model's coding factor equalisation made it possible to distinguish between the factor coefficients and determine their proportional influence. The F-value of 44.27 and the p-value of 0.0003 show that the result of the % transmittance model is significant. The adjusted experimental % Transmittance ME10 of 96.48 is quite consistent with the predicted % Transmittance ME10 of 97.001.

Response3: For the drug release at 6 hours, quadratic model D optimal was used for the prediction of drug release at 6 hours. The results of the drug release at 6 hours are predicted by the F-value of 49.36 and the p-value of 0.0002, respectively. Model is significant since the statistical model equalisation regarding coded components allowed in order to separate the component coefficients and determine the relative significance. The anticipated drug release at 6 hours ME10 of 95.146% and the modified experimental drug release at 6 hours ME10 of 96.25% are reasonably in agreement.

Optimized formulation ME10: ME10 prepared on the amount of percentage of IPM 3.831%, S-MIX 0.919 %, Water 0.250 %. Physicochemical evaluations were performed globule size was about 219.56 nm, % transmittance 97.001 and drug release at 6 hour is 95.146%.

Analysing the Optimized Formulation ME10 Quinine Sulphate Microemulsion experimental (E) and Predicted (P) values

The predicted values for optimized formulation ME10 quinine sulphate microemulsion was found to be globule size 219nm, Transmittance 97.001 and drug release at 6 hr is 95.146%.

The experimental values for quinine sulphate microemulsion was found to be Globule size 212 nm, Transmittance 96.48 and drug release at 6 hr is 96.254%

Physical appearance: ME1, ME2, ME3, ME4, ME5, ME6, ME7, ME8, ME9 Shows Clear.

% Transmittance:

The microemulsion formulation % transmittance ranged from 95.48% to 99.25 %. ME1 Shows 97.92% ME2 98.37%, ME3 98.68%, ME4 97.4%, ME5 96.23%, ME6 96.74%, ME7 95.48%, ME8 95.97%, ME9 99.25%. The

transmittance value of ME2, ME3, and ME9 is more than 98%. According to these results, microemulsion has a high level of clarity. A microemulsion's transparency and %Transmittance measurements may be affected by oil globules because of their greater particle size.

Invitro drug diffusion release: Finally, the microemulsions in vitro diffusion experiments in phosphate buffer pH 7.4 were assessed. Formulations ME1 releases 94.64 % at 6 hours, ME2 at 93.57%, ME3 at 91.56%, ME4 at 92.49 %**,** ME5 at 96.49 %, ME 6 at 95.79%, ME 7 at 98.63%, ME 8 at 97.54%, ME 9 at 90.79 %. ME7 shows higher drug release compared to other microemulsion formulations.

Thermal stability:

S.no	Formulation	Heating / Cooling cycle	Freeze thaw cycle	Centrifugation	Inference
1	ME1	+	+	+	Pass
2	ME2	+	+	+	Pass
3	ME3	+	+	+	Pass
4	ME4	+	+	+	Pass
5	ME5	+	+	+	Pass
6	ME6	+	+	+	Pass
7	ME7	+	+	+	Pass
8	ME8	+	+	+	Pass
9	ME9	+	+	+	Pass
10	ME10	+	+	+	Pass

+ Pass, No phase separation - Fail, Phase separation

It was discovered ME1- ME10 formulations were stable under centrifugation, heating/cooling cycles, and freeze thaw test due to phase separation selected for characterization and evaluations.

Preparation of Quinine sulphate micro emulsifying suppositories

Formulation of suppository involves adding of melted cocoa butter along with microemulsion through the fusion method. 1.5gm of the drug is added in 10ml of the microemulsion, and 0.1 ml of the microemulsion is added in each suppository to get 15 mg of the drug in each suppository.

Total of 12 suppositories were prepared and 10 suppositories are weighed and variation calculated and 6 suppositories were evaluated for disintegration time, Melting time, Liquefication time, invitro diffusion and dissolution studies.

Suppositories with microemulsion MES1-637mg, MES2-674mg, MES3-606mg, MES4-614mg, MES5-598mg, MES6-619mg, MES7-641mg, MES8-665mg, MES9-678mg, MES10-628mg. Total weight of suppositories with microemulsion was 6.374gm

Suppositories without microemulsion MES1-601mg, MES2-647mg, MES3-651mg, MES4-624mg, MES5-625mg, MES6-704mg, MES7-683mg, MES8-606mg, MES9-651mg, MES10-582mg. Total weight of suppositories without microemulsion was 6.358gm

Determination of displacement values:

Prepare and measure 10 cocoa butter-containing suppositories: A gram=6.358gm

Make 10 suppositories with 40% medicament and weigh them: B gram=6.374gm

Determine the base content of the medicated suppository: (60/100) ×B = C gram=3.824gm

Determine the quantity of medication in the medicated suppository: (40/100) ×B = D gram=2.549gm

Estimate the amount of base that D grams of medication shifts: (A-C) gm

DV of drug = D/ (A-C) =1.005

Preparation of Quinine sulphate microemulsion based suppository without microemulsion drug and with microemulsion drug

Physical evaluation: The Quinine sulphate micro emulsifying suppository MES1, MES2, MES3, MES4, MES5, MES9 and MES10 shows yellow colour, MES6, MES7, MES8 Shows Pale yellow colour. All the suppositories are Smooth surface in condition.

Uniformity of weight: The weight variation of suppositories was found to be MES1 -36.4mg, MES2 +9.6mg, MES3 +13.6mg, MES4 -13.4mg, MES5 -12.4mg, MES6 +66.6mg, MES7 +45.6mg, MES8 -31.4mg, MES9 +13.6mg, MES10 -55.4mg.

The Percentage deviation of suppositories was found to be MES1=5.71, MES2=1.50, MES3=2.13, MES4=2.10, MES5=1.94, MES6=10.44, MES7=7.15, MES8=4.92, MES9=2.13, MES10=8.69.

Disintegration time: The Time taken for formulated micro emulsifying suppository to disintegrate and go into solution. The disintegration time was found to be MES1-18.03 min, MES2-17.49 min, MES3-26.26min, MES4-19.17min, MES5-16.41 min, MES6-19.30min.

Liquefication time (softening time) and Melting range at 35 ± 0.2°C.

The Liquefication time was found to be MES1-12±1.001, MES2-15±1.723, MES3-13±2.642, MES4- 6±1.0, MES5-13±0.567, MES6-21±1.943. All the micro emulsifying quinine sulphate suppository showed liquefication time in range of 6 to 21 min. The Melting time was found to be MES1- 7 min 41 sec, MES2- 4 min 28 sec, MES3- 5 min 36 sec, MES4- 5 min 28 sec, MES5- 3 min 46 sec, MES6- 4 min 22 sec. All the quinine sulphate micro

emulsifying suppositories with stand body temperature at 35 ± 0.2°C aids in the simple handling and release of medication following rectal administration.

In vitro dissolution studies: Drug dissolution profile of pure drug Quinine sulphate and micro emulsifying suppositories using Cocoa butter were studied by using phosphate buffer at a pH of 7.4 as the dissolving media. The drug release at 30 minutes for micro emulsifying suppositories was found to be MES1-94.78%, MES2-97.52%, MES3-92.37%, MES4-98.75%, MES5-94.71%, MES6-97.36%. Among all the micro emulsifying suppository formulation the maximum dissolution of 98.75% in 30 min and minimum dissolution of 92.37% in 30 min. Formulation MES4 shows better dissolution rate than the rest of micro emulsifying suppositories. Formulation MES3 showed slowest dissolution rate when compared to other micro emulsifying suppositories.

Invitro diffusion studies: The drug release profile was studied for all formulated Quinine sulphate micro emulsifying suppositories in Franz diffusion cell. The drug release at 6 hours for micro emulsifying suppositories were found to be MES1-84.13%, MES2-87.08%, MES3-81.44%, MES4-90.4%, MES5-83.89%, MES6-90.15%. Among all the micro emulsifying suppository formulation the maximum diffusion of 90.40% in 30 min and minimum dissolution of 81.08% in 30 min. Formulation MES4 shows better dissolution rate than the rest of micro emulsifying suppositories. Formulation MES3 showed slowest diffusion rate when compared to other micro emulsifying suppositories.

Discussion

The use of Spans/Tweens was used to produce MEs. The additional surfactant Span 20 was selected. The highest water-to-oil ratio that could be produced for the microemulsion was employed to evaluate the surfactant's effects. (18) An effort was made to create a microemulsion using isopropyl myristate and ethanol after studying the European, US, and Japanese Pharmacopoeias (EP, USP, and JP, respectively). Rectal dose forms are covered in a distinct chapter named "Rectal preparations/Rectalia" in only the EP. Rectal preparations are "systems intended for rectal use to elicit a systemic or local effect," according its definition. They might also be utilised for diagnostics. (19)

Rectal dosage forms are not specifically covered in the USP or JP, despite the fact that the suppository dose form is described. The USP refers to suppositories as dose forms often utilised in the rectum. These suppositories may

contain hard fats, polyethylene glycol combinations, glycerinated gelatin, hydrogenated vegetable oils, cocoa butter, and polyethylene glycol fatty acid esters. (20)

Despite their benefits for rectal medicine administration, traditional suppositories have drawbacks include inconsistent drug absorption, leaking, and aches and pains. These solid dosage forms now offer significantly improved bioavailability, formulation retention, and patient suitability. To create solid emulsion-type suppositories, this here with microemulsion-containing surfactants to either the hydrophilic or lipophilic phase of the formulation (examples include polysorbate 80, Tween 20, and Span 60). (21)

As PEG gradually dissolves in the dissolving fluid, the drug is released from the PEG suppositories. PEG (P1-P4)-based suppositories produced a maximum 90 percent release during the first 30 minutes. The rate and quantity of drug absorption in the body are influenced by the nature of the drug substance, the composition of the suppository base, and the rectal environment, and this is why microemulsion-based suppositories containing quinine sulphate show a maximum 98.75% dissolution rate in dissolution studies within a 30-minute window. (22)

The liquefication times for all the quinine sulphate micro emulsifying suppositories were between 6 and 21 minutes. It is the period that micro emulsifying suppositories can tolerate body temperature at 37°C, making it easier to handle and release the medicine after use.

CONCLUSION: Quinine sulphate belongs to an antimalarial drug of BCS class II used to treat malaria. Therefore, the present investigation is concern with the developing the micro emulsifying suppository.

The following conclusions were drawn from results obtained:

- When compared to other oils, surfactants, and CO surfactants, isopropyl myristate (96.32%), Span 20 (96.32%), and ethanol (44.64%) were shown to have the highest solubility of quinine sulphate. Thus, they were selected for the development of the microemulsion formulation.
- The developed microemulsion formulations ME1, ME2, ME3, ME4, ME5, ME6, ME7, ME8, ME9, and ME10 all passed a test for thermodynamic stability.
- The average microemulsion formulation % transmittance was determined to be about 95.48 - 99.25% respectively

- The ME10 microemulsion is the best formulation, as per comparisons of Invitro release of drug, average globule size, amount of surfactant, and stability tests, which found that there is no appreciable change in microemulsion characteristics under various storage circumstances.
- Among the formulated micro emulsifying suppositories, the formulation MES4 gave the best results, MES4 showed the maximum dissolution of 98.75% in 30 min with a disintegration time 19.17 min and drug release 90.40% in 6 hours in diffusion studies. Even from the stability studies data it can be concluded that MES4 showed least change in appearance when stored under different conditions such as room temperature (28°C), refrigerator temperature (4° C) even after 4 weeks of period.
- The formulation MES 3 showed the lowest drug release 92.37% in 30 min in dissolution with disintegration time 26.26 min and drug release 81.44 % in 6 hours in diffusion studies. The slow drug release is possibly due Composition of Cocoa butter and Micro emulsifying drug in micro emulsifying Suppository.
- All the formulation (MES1- MES6) micro emulsifying suppository evaluated showed comparable dissolution & drug release results with MES4 is best, since 98.75% drug dissolved in 30 min in dissolution studies and 90.38% drug release in 6 hours in diffusion studies

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Abbreviations

% - Percentage

% T – Percentage transmittance

> - Higher than

gm- Gram

ml - Millilitre

mg- Milligram

Kg- kilogram

T½- Half-life

pH- Hydrogen ion concentration

°C- Degree Celsius

T- Turbidity

C- Clear

ME-Microemulsion

MES- Micro emulsifying suppository

S mix - Surfactant and cosurfactant mix

PEG- Polyethylene glycol

IPM - Iso propyl myristate