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# Formulation and in vitro evaluation of Vincristine microemulsion by using nigella sativa oil

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## ABSTRACT

Vincristine is an anti-metabolite having an anti-cancer its having low aqueous solubility hence formulated microemulsion will increase its solubility and thus improves the oral bioavailability selection of nigella sativa oil is due to its anti-cancer property and the solubility of drug in oil (70mg/ml).micro emulsion was prepared by phase titration method using nigella sativa oil, tween 80, tween 20, water..8blank formulations were formulated based on various physical parameters clarity, stability, density, viscosity, ph, and electrical conductivity,3formulations were narrowed down, drug loaded in previously selected blank microemulsion formulation the particle size study was carried out by zeta analysis and the results proved that the formulations were micron sized. Ftir studies proved that there was not much interaction between the drugs in the formulation. *In-vitro* dissolution studies were performed for all the 17 formulations individually for both the drugs was found. The optimized formulation was sustained release this formulation was subjected to *ex-vivo* diffusion study and the permeation through the membrane was found.

**Keywords:** Nigella sativa oil, Electrical conductivity, Microemulsion.

## INTRODUCTION

Oral route is the simplest and easiest way to administer drug for reasons of convenience of administration, greater stability, smaller bulk, accurate dosage, ease of production and easy compliance [1]. Therefore, most of the new chemical entities (NCE) which are under development these days, are intended to be used orally that reproduces an effective *in vivo* plasma concentration after oral administration.

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body [1, 2]. Cancer is fundamentally a disease of tissue growth regulation, the genes that regulate cell growth and differentiation must be altered. Inappropriate over-expression of normal oncogenes, or by the under-expression or disabling of tumor suppressor genes. Typically, changes in multiple genes are required to transform a normal cell into a cancer cell.

Vincristine is white solid crystalline powder .It is a plant alkaloid derived from a plant vincarosea act as anti-neoplastic agent [3]. The molecular weight of vincristine is 824.9576.It is an approved drug and over the counter drug administered weakly by iv infusion and it undergo hepatic metabolism.it is insoluble in water has 0.03mg/ml water solubility, IUPAC name is methyl (1R,9R,10S,11R,12R,19R)-11-(acetyloxy)-12-ethyl-4-[(13S,15S,17S)-17-ethyl-17-hydroxy-13-(methoxycarbonyl)-1,11-diazatetracyclo nonadeca-4(12),5,7,9-tetraen-13-yl]-8-formyl-10-hydroxy-5-methoxy-8,16-diazapentacyclononadeca-2,4,6,13tetraene-10-carboxylate its melting point is 220 °C it is used in acute lymphocytic leukemia (ALL), Hodgkin lymphoma, non-Hodgkin lymphomas, Wilms' tumor, neuroblastoma, rhabdomyosarcoma or solid tumors associated with an ability to destabilize the

microtubules by binding to tubulin and blocking the polymerization inhibit the mitosis thereby arresting the cell division. Nigella Sativa oil is Brown to deep brown free flowing liquid having anti cancer property and studies revealed that it is potent than cisplatinand it act as a good carrier of vincristine is having poor oral bioavailability micro emulsion is novel drug delivery techniques used to improve the dissolution rate of poorly water soluble drugs micro emulsion used as an edge of potential drug delivery vehicle because of their thermodynamic stability, reversibility, simple manufacturing scale up feasibility, and do not require any special equipment oil in water micro emulsion is the most suitable formulation which is expected to increase the solubility in to an oil phase thus vincristine considered to be the good candidate for micro emulsion drug delivery system to enhance its oral bioavailability.

## MATERIALS AND METHODS

All the chemicals obtained and used are of analytical grade. Vincristine obtained from cipla labs, Nigella sativa oil obtained Mohammedia products. co,shahalibanda ,Hyd. Tween 20, Tween 80, Tween 85, water, obtained from Research-lab fine chem. Industries, Mumbai.

## METHODS

### Preparation of Blank formulation

The O/W microemulsion formulations were prepared by phase titration method [4]. Surfactants water ratios were taken as constant (60:40 respectively) and varying concentrations of oil and water.

The formulations were prepared by blending Tween 85,Tween,20,Tween80,at predetermined HLB values Spontaneous emulsification was then applied by mixing deionized water with appropriate surfactant blends at different ratios (Table 1) using magnetic stirrer for 10 minutes at 640 rpm. After that, the N. sativa oil was titrated drop-wise until a transparent solution was formed [5]. Only formulation that appeared transparent was further characterized and subjected to stress-testing at room temperature for at least 24hrs and observed or examined for signs of turbidity or phase separation prior to further studies. The prepared formulation is then kept aside.

**Table 1: Different blank formulations**

| Code | Qty. of oil NS oil (%) | Vol. of aqueous phase (%) | Qty. of surfactant (%) | Surfactant blend |
|---|---|---|---|---|
| NT1 | 16.7 | 27.8 | 55.5 | 60% T20 / 40% T85 |
| NT2 | 11.4 | 12.7 | 75.9 | 60% T20 / 40% T85 |
| NT3 | 15 | 25 | 60 | 60% T20 / 40% T85 |
| NT4 | 13.8 | 17.2 | 69 | 60% T20 / 40% T80 |
| NT5 | 13 | 22 | 65 | 60% T20 / 40% T80 |
| NT6 | 10.7 | 17.9 | 71.4 | 60% T20 / 40% T80 |
| NT7 | 9.1 | 18.2 | 72.7 | 60% T20 / 40% T80 |
| NT8 | 7.4 | 18.5 | 74.1 | 60% T20 / 40% T80 |

### Drug loaded microemulsion formulation

The drug loaded microemulsion formulations were prepared by incorporating the drugs [Vincristine] in the previously prepared blank formulations [6]. The drug content was then calculated by performing the assay of the drugs spectrometrically at 303 nm.

Firstly drug was dissolved in N.sativa oil then the prepared surfactant blends were mixed with water using magnetic stirrer for 10 min, after that N.sativa oil containing drug was titrated drop wise until transparent solution was formed.

**Table 2: Different drug loaded formulations**

| Code | Qty. of drug(mg) Vincristine | Qty of oil (ml) N.Sativa | Vol. of aqueous phase (%) | Qty. of surfactant (%) | Surfactant blend |
|---|---|---|---|---|---|
| ME1 | 30 mg | 10.7ml | 17.9 | 71.4 | 60% T20 / 40% T80 |
| ME2 | 30 mg | 9.1ml | 18.2 | 72.7 | 60% T20 / 40% T80 |
| ME3 | 30 mg | 7.4ml | 18.5 | 74.1 | 60% T20 / 40% T80 |

## Evaluations methods

## Physical parameters

### Visual Observation

Visual observation of the prepared formulations was analyzed. **Parameters** such as **Transparency, Phase Separation** are included and the formulations which have better clarity and with no phase separation were confirmed for selection as clarity of the formulation is the initial priority of the microemulsion.

### pH

The pH of the prepared 32 microemulsion formulations was determined by using pH meter. The pH was determined by bringing the electrode in contact with the formulations allowing it to equilibrate for a minute [7]. Initially the pH meter was calibrated with suitable calibration solution of pH 4.9 and 7.9 by water. The formulations with pH ranging between 4.5 and 7.5 were confirmed for selection as this range was neither too acidic nor too basic.

### Density

The density of the prepared O/W microemulsion formulations was determined using a typical Picnometer. The empty weight of the picnometer is noted. Water is taken up to the neck of the picnometer and the weight is determined by using electronic balance. Now the difference between the total weight and empty picnometer weight would give the weight of water. Then, the volume of the water that was filled up to the neck was noted which is the volume of the picnometer [8]. The density of water is then calculated. Then, the prepared microemulsion formulations are taken in the picnometer and the weight is calculated. As the volume is known, the density of the formulations was calculated by the formula,

$$\text{Density [g/mL]} = \frac{\text{weight(g)}}{\text{volume[ml]}}$$

### Viscosity

The viscosity of the microemulsion formulations was determined by Brookfield Viscometer using spindle. The viscosity of the microemulsion formulations was determined at various 10, 20, 50, 100, 150, 200 rpm operating at 37ºC. Lesser the viscosity, better the administration of the formulation, since less viscous formulations have a better flow property than the high viscous formulations [9]. Hence, less viscous formulations were confirmed for selection.

### Electrical Conductivity

The electrical conductivity [10] of the formulations was determined by a conductivity meter. Initially, the conductivity meter is calibrated with distilled water and then, the conductivity is obtained by bringing the electrode in contact with the formulations. The electric conductivity was calculated in microSiemens [μS].

## Particle size analysis

### Zeta Potential and Globule Size

The particle size [11] or the globule size of selected formulations was analysed using zeta-size analysis. A graph was plotted for size in nm against % of intensity.

The size where there was maximum intensity was observed is the mean globule size of the formulations. Droplet size was calculated using the Stokes-Einstein relationship by Zeta sizer Software. Electrophoretic mobility (μm/s) was measured using small volume disposable zeta cell and converted to zeta potential by in-built software using Helmholtz–Smoluchowski equation. Particle size analysis was performed to confirm that the formulations were of micro-size range.

### Drug Content

A specific quantity (100mg) of developed microemulsion is taken and dissolved in 100ml of phosphate buffer of pH 6.8. The volumetric flask containing gel solution was shaken for 2hr on mechanical shaker in order to get complete solubility of drug. This solution was filtered and estimated spectrophotometrically at 303.0nm using phosphate buffer (pH 6.8) as blank.

### Transmission electron microscopy (TEM)

Morphology and structure of the microemulsion were studied using transmission electron microscopy TOPCON 002B operating at 200 KV (Topcon, USA) and capable of point to point resolution. Combination of bright field imaging at increasing magnification and of diffraction modes was used to reveal the form

and size of microemulsion droplets. In order to perform the TEM observations, a drop of the microemulsion was directly deposited on the holey film grid and observed after drying.

## Fourier Transform Infrared Spectroscopy [FTIR]

FT-IR (MacDonald et al., 1986) was performed in order to find out the compatibility between the drugs in the formulation and also the drugs with other excipients. Analysis was done on vincristine drug and the combined drug in the formulation. vincristine were analyzed by KBr pellet technique in which the sample was dispersed in KBr and compressed into discs by applying a pressure 5 t for 5 min in a hydraulic press. The pellet was placed in the path of infrared rays and the spectrum was recorded. The formulation containing both the drugs was analyzed by ATR where the liquid sample is directly placed on the ATR crystal and subjected to IR rays. A beam of infrared light is passed through the ATR crystal in such a way that it reflects at least once off the internal surface in contact with the sample. The sample absorbs energy and the spectrum was recorded. The samples were scanned in the wave number range from 4000 cm-1 to 400 cm-1.

## *In-vitro* Dissolution studies

Among the 8 formulations, 3 formulations [F6 to F8] were selected on the basis of transparency, pH, Density, Viscosity and Conductivity and concentration of Co-surfactant and were subjected to *in-vitro* [12] dissolution in order to analyze the release pattern of the selected O/W microemulsion formulations in the dissolution apparatus using a dialysis membrane. Dialysis membrane was tied at one end of an open ended tube of dimensions 10mm diameter and 20 mm height and 1mL of formulation is poured through the other end and made to be in contact with the membrane. This tube setup is placed in the basket and subjected to dissolution with 100mL water being the media where the media is made to be in contact with the membrane. The other dissolution parameters include temperature of 37ºC at 50 rpm. The dissolution process is carried out for 6 hours to check sustained release and the samples taken at regular Intervals and replaced with the same quantity of fresh media to maintain the sink condition and the samples were analyzed spectrophotometrically at 303 nm. The percentage drug release was calculated using standard calibration curve and the graphs were plotted by taking percentage drug release along the Y-axis and time along X-axis to compare release with respect to time.

## *Ex-vivo* Diffusion studies

From the results obtained in the dissolution analysis, one formulation where sustained release was recorded for both the drugs was continued for *ex-vivo* [13] diffusion studies. This study was carried out in KesharyChein type diffusion cell using distilled water as the diffusion media. The diffusion cell comprised of a donor and a recipient compartment with a capacity of 5mL and 20 mL respectively. Fresh mucous membrane obtained from goat skin was used as the membrane and the formulation was analyzed for permeation in a natural membrane. 20 mL of distilled water was filled in the recipient compartment and 1 mL of the individual drug loaded formulation was placed in the donor compartment. The diffusion cell was setup on a magnetic stirrer and maintained at 37ºC. Sample was taken at regular time intervals and was replaced by the same quantity of fresh diffusion media in order to maintain the sink condition. The study was continued for 6 hours and the % drug release was calculated using standard calibration curve and the graphs wereMplotted by taking %drug release along the Y-axis and time along X-axis to compare release with respect to time.

## Kinetic Modelling study of dissolution data

Drug release kinetics study helps us in understanding the release pattern and mechanism behind them. There are several linear and non- linear kinetic models available which are classified as Zero order, First order, Higuchi model, Korsmeyer Peppas and Hixson Crowell model. To analyze the drug release mechanism of the formulations data obtained were fitted with these models and the best fit was recorded. Each model follow different rule of kinetic analysis module based on which release pattern are calculated

## Thermodynamic Stability Studies

Selected formulations were subjected to different thermodynamic stability tests to assess their physical stability.

1. Heating–cooling cycle: Six cycles between refrigerator temperature (4°C) and 45°C with storage at each temperature of not less than 48 h were conducted, and the formulations were examined for stability at these temperatures.
2. Centrifugation test: Formulations were centrifuged at 3,500 rpm for 30 min, and we looked for phase separation.
3. Freeze–thaw cycle: Three freeze–thaw cycles between −21°C and +25°C, with formulation storage at each temperature for not less than 48 h, were performed.

### Dispersibility Test

The thermodynamically stable microemulsions were further taken for the dispersibility test for visual assessment and were assessed using following grading system:

- Grade A: Rapidly forming (within 1 min) microemulsion, having a clear or bluish appearance.
- Grade B: Rapidly forming, slightly less clear microemulsion, having a bluish white appearance.
- Grade C: Fine milky microemulsion that formed within 2 min.

### Robustness to Dilution

Microemulsions resulting from dilution with dissolution media must be robust to all dilutions and should not show any separation even after 24 hours of storage

## RESULTS AND DISCUSSIONS

### FTIR

### IR Spectrophotometry

FTIR analysis of all the excipients used in the formulation and the drug were studied for the interaction of the excipients and the drug in the formulation.The obtained spectrums of different surfactants & Oil were showed no degradation of drug formulationPure vincristine spectra showed sharp characteristic peaks at 3400, 1300 and 1200cm−1.

The nature of peak did not vary in microemulsion formulation indicate that there was no interaction between the drug and excipients(i.e surfactants & Oils) in the formulation.The graphs of excipients,drug and final formulation are shown in the Fig 1,2.

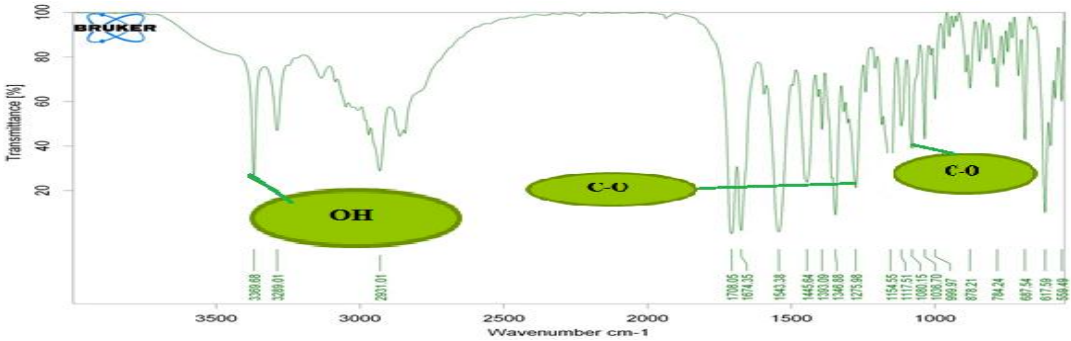



**Fig 1: IR spectrumof vincristine drug**

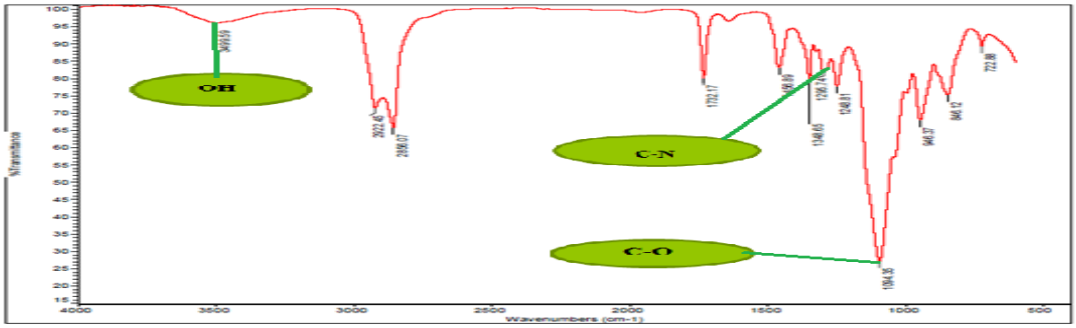



**Fig 2: IRSpectrumof Microemulsion of vincristine**

## Transparency, pH, Density, Viscosity and Conductivity

The transparency, pH, Density, Viscosity and Conductivity of the 8 formulations were determined. Based on these parameters, the formulations are screened and narrowed down to 17 efficient formulations. They are tabulated as follows. Transparency increased with the increase in the concentration of surfactant. Increase in the surfactant changed the color of the formulation but not the clarity. NT6, NT7, NT8 provided greater transparency at different concentration of co surfactants. NT6, NT7, and NT8 had pH of around 8.0, 7.4 and 7 respectively. Increase in the surfactant concentration, decreased the conductivity. Since the surfactants contain lipophilic groups, the conductivity would eventually decrease with increase in the surfactant concentration. Density had no extreme variations. Decrease in the concentration of co-surfactants, increased the density. Based on these parameters, 3 formulations were selected for further evaluation.

**Table 3: Physical parameters of 8 O/W microemulsion formulations**

| Formulation Code | Appearance | pH | Density[gm/ml] | Viscosity[cP] at 100 rpm | Conductivity [Ms/cm] |
|---|---|---|---|---|---|
| **NT1** | Slightly Cloudy | 8.1 | 1.01 | 2.21 | 0.68 |
| **NT2** | Slightly Cloudy | 8.0 | 1.01 | 2.18 | 0.64 |
| **NT3** | Translucent | 8.0 | 1.03 | 2.14 | 0.61 |
| **NT4** | Transparent | 7.8 | 1.04 | 2.12 | 0.59 |
| **NT5** | Transparent | 7.8 | 1.07 | 2.08 | 0.57 |
| **NT6** | Transparent | 7.7 | 1.08 | 2.04 | 0.55 |
| **NT7** | Transparent | 7.4 | 1.11 | 1.48 | 0.43 |
| **NT8** | Transparent | 7.0 | 1.13 | 1.14 | 0.30 |

**Table 4: Physical parameters of selected drug loaded microemulsion**

| Formulation Code | Appearance | pH | Density[gm/ml] | Viscosity [cp]@100 rpm | Conductivity(micro Siemens) | % Assay |
|---|---|---|---|---|---|---|
| **ME1** | Transparent | 7.7 | 1.08 | 2.04 | 0.55 | 99.5 |
| **ME2** | Transparent | 7.4 | 1.11 | 1.48 | 0.43 | 98.36 |
| **ME3** | Transparent | 7.0 | 1.13 | 1.14 | 0.30 | 99.7 |

## *In-vitro* release studies

**Table 5: In-vitro cummulative % drug release profile for Vincristine Microemulsion**

| Time (min) | VNTT14 | VNTT15 | VNTT16 |
|---|---|---|---|
| 30 | 68.48 | 64.4 | 41.68 |
| 60 | 83.02 | 73.3 | 53.3 |
| 120 | 92.6 | 99.3 | 57.7 |
| 180 | 99.7 | - | 64.4 |
| 240 | - | - | 70.6 |
| 300 | - | - | 82.6 |
| 360 | - | - | 93.7 |

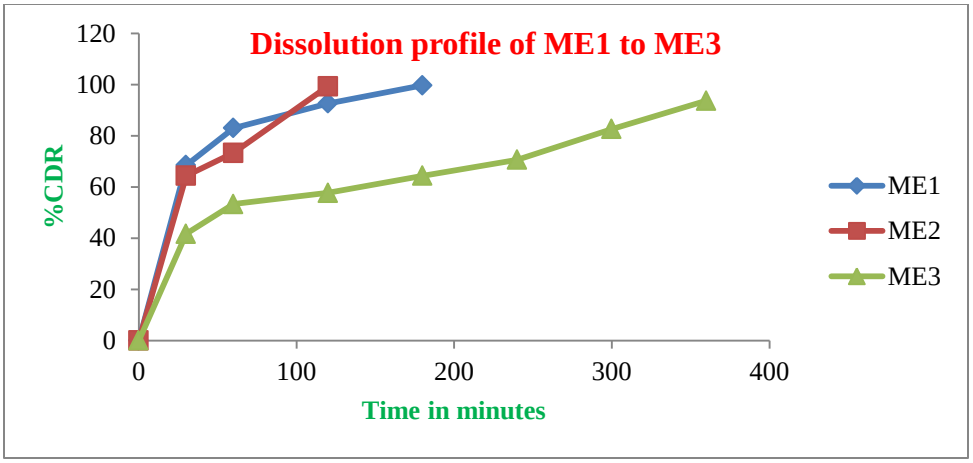



**Fig 3 : Dissolution profile of ME1 to ME3**

## Dissolution profile of ME1, ME2 and ME3

From the release data of vincristine miceoemulsion, only one i.e., ME 3 showed nearly 100% drug release after 6 hours rest of the formulation shows difference in drug release. So ME 16 was chosen.

## Ex vivo Diffusion studies

Distilled water was used for *in vitro* release as a receptor medium. The pretreated skin of intestinal membrane was used in fraz diffusion cell. The sample was applied on the membrane and then fixed in between donor and receptor compartment of diffusion cell. The receptor compartment contained Distilled water (20ml) of water. The temperature of diffusion medium was thermostatically controlled at 37º ± 1º by surrounding water in jacket and the medium was stirred by magnetic stirrer at 500rpm. The sample at predetermined intervals were withdrawn and replaced by equal volume of fresh fluid. The samples withdrawn were spectrophotometrically estimated at 303nm against their respective blank.

**Table 6: Ex vivo Diffusion studies of ME3**

| S.no. | Time interval | % Drug release ME3 |
|---|---|---|
| 1 | 30 | 31.21 |
| 2 | 60 | 42.1 |
| 3 | 120 | 59.3 |
| | 180 | 67.4 |
| 4 | 240 | 76.6 |
| 5 | 300 | 80.3 |
| 6 | 360 | 86.7 |

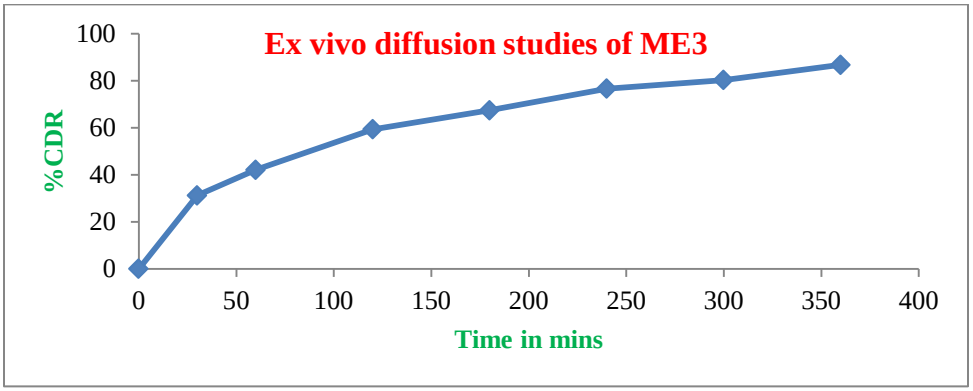



**Fig 4: Ex vivo diffusion studies of ME3**

ME3 found to be a better formulation for the release of drugs. From the ex vivo evaluations, the data showed that formulation could be effectively used for sustained release of vincristine kinetic release models.

**Table 7: Release kinetics for ME3**

| Parameters | ZERO<br>% CDR Vs T | FIRST<br>Log % Remain Vs T | HIGUCHI<br>%CDR Vs √T | PEPPAS<br>Log C Vs Log T |
|---|---|---|---|---|
| **Slope** | 11.75406162 | -0.156689071 | 33.37776317 | 0.810015361 |
| **Intercept** | 26.40845938 | 2.179286808 | 9.85454561 | 1.333436687 |
| **Correlation** | 0.898170314 | -0.942339644 | 0.971574651 | 0.437904325 |
| **R 2** | 0.806709913 | 0.888004005 | 0.943957302 | 0.191760198 |

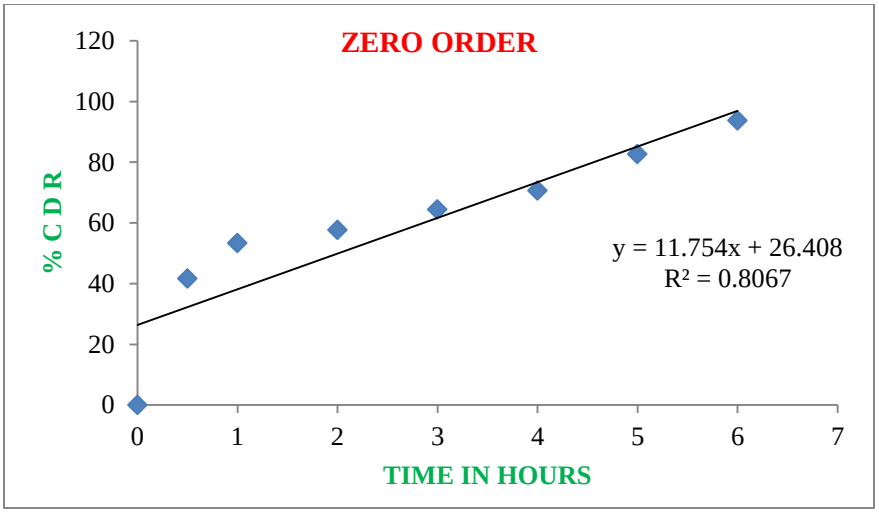



**Fig 5: Zero order release graph for ME3**

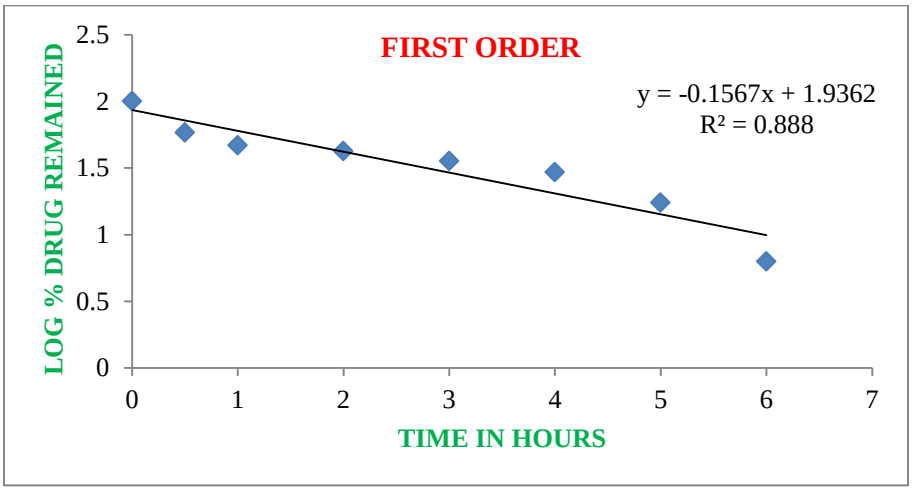



**Fig 6 : First order release graph for ME3**

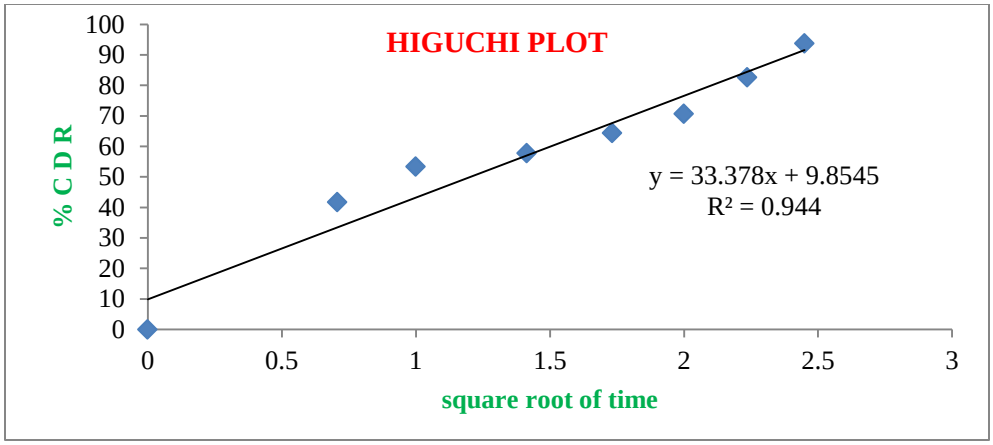



**Fig 7 : Higuchi model graph for ME3**

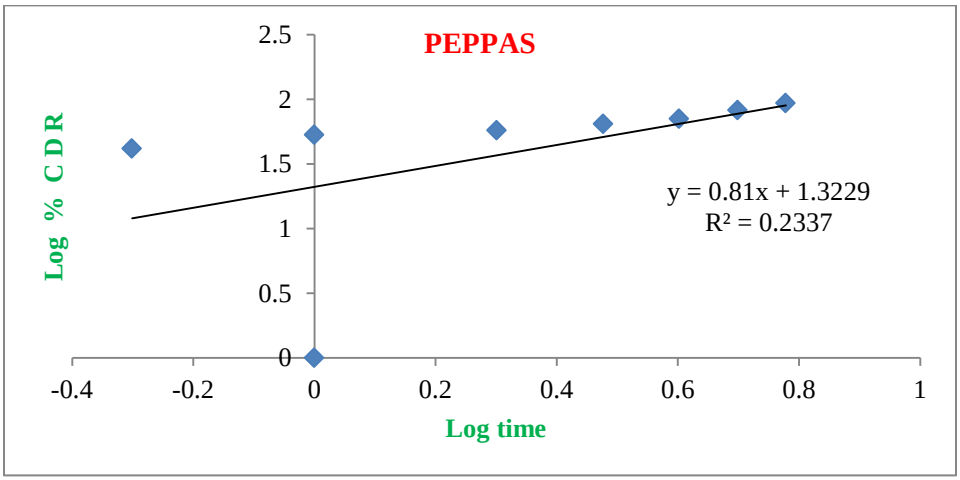



**Fig 8 : Peppas model for ME3**

**Transmission Electron Microscopy**

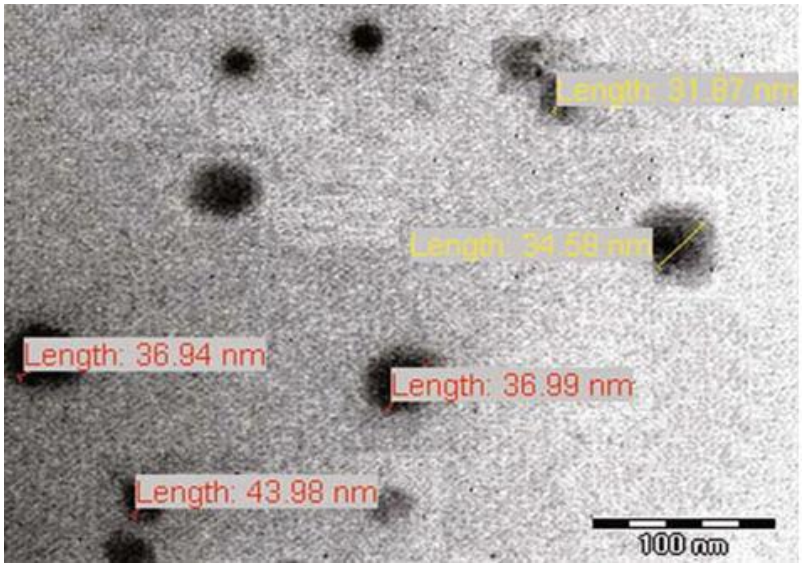
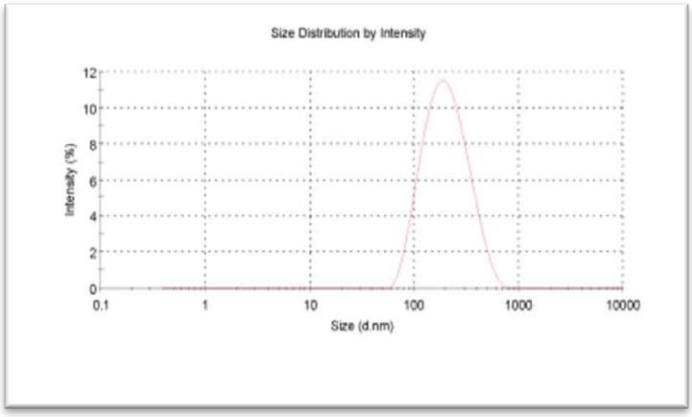



**Fig 9 : TEM image of vincristine microemulsion ME3**

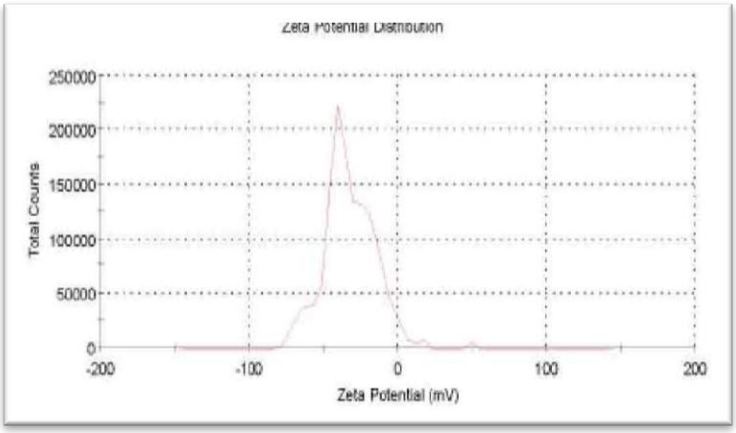
**Zeta Sizer**

The Size of the microemulsion droplet size was found to be 32.1nm in diameter with the help of zeta sizer with a zeta potential of -13.1.

| **Results size(d.nm):** | **%Intensity** | | **Width(d.nm)** |
|---|---|---|---|
| **Z- AVERAGE (D.NM): 32.1** | **Peak1: 38.4** | **100** | **106.8** |
| **PdI: 0.168** | **Peak2:** | **--** | **--** |
| **Intercept: 0.96** | **Peak3:** | **--** | **--** |
| **Result quality**: **goo** | | | |




| **Resultssize(d.nm):** | **%Intensity** | **Width(d.nm)** | |
|---|---|---|---|
| **Zeta Potential (mV): -13.61** | **Peak1:-13.1** | **98.5** | **16.4** |
| **Conductivity (mS/cm): 1.24** | **Peak2:--** | **--** | **--** |
| **Result quality**: good | **Peak3:--** | **--** | **--** |




## Thermodynamic stability

Microemulsions are thermodynamically stable systems and are formed at a particular concentration of oil, surfactant and water, with no phase separation, creaming or cracking. It is the thermo stability which differentiates micro- or microemulsion from emulsions that have kinetic stability and will eventually phase separate. Thus, the selected formulations were subjected to different thermodynamic stability by using heating cooling cycle, centrifugation and freeze thaw cycle stress tests. Those formulations, which survived thermodynamic stability.

**Table 8: Thermodynamic stability of VNTTM14 - VNTTM16**

| Formulation Code | Observation | | | Inference |
|---|---|---|---|---|
| | Heating/Cooling | Centrifugation | Freeze thaw | |
| VNTTM14 | ✓ | ✓ | ✓ | PASSED |
| VNTTM15 | ✓ | ✓ | ✓ | PASSED |
| VNTTM16 | ✓ | ✓ | ✓ | PASSED |

### Drug Content

A specific quantity (100mg) of developed microemulsion is taken and dissolved in 100ml of phosphate buffer of pH 6.8. The volumetric flask containing gel solution was shaken for 2hr on mechanical shaker in order to get complete solubility of drug. This solution was filtered and estimated spectrophotometrically at 303.0nm using phosphate buffer (pH 6.8) as blank.

### Accelerated Stability Studies

All the selected formulations were subjected to a stability testing for three months as perICH norms at a temperature of 40º ± 2º. All selected formulations were analyzed for the change inappearance, pH or drug content by procedure stated earlier.

**Table 9: Accelerated Stability Studies of ME1 – ME3**

| S. no. | Batches | Months | Appearance | pH | Drug content (%) |
|---|---|---|---|---|---|
| 1 | **ME1** | 0 | Clear | 6.8 | 99.95 |
| | | 1 | Clear | 6.8 | 98.60 |
| | | 2 | Clear | 6.7 | 97.00 |
| | | 3 | Clear | 6.6 | 96.20 |
| 2 | **ME2** | 0 | Clear | 6.8 | 99.94 |
| | | 1 | Clear | 6.6 | 98.50 |
| | | 2 | Clear | 6.6 | 97.40 |
| | | 3 | Clear | 6.5 | 96.30 |
| 3 | **ME3** | 0 | Clear | 6.8 | 99.98 |
| | | 1 | Clear | 6.8 | 98.80 |
| | | 2 | Clear | 6.8 | 97.30 |
| | | 3 | Clear | 6.6 | 96.80 |

## CONCLUSION

A microemulsion system for the oral delivery of vincristine was prepared using a series of oils, surfactants and co-surfactants. Initially 8 BLANK formulations were prepared and tested for their transparency, density, viscosity, DISPERSIBILITY and conductivity. Based on these parameters, 3 formulations were selected and further continued for solubilizing capacity and *invitro* dissolution, evaluation. From the obtained data from dissolution evaluation, one formulation which had the capacity of releasing the drug in sustained manner was selected. The formulation was ME3 and it had the components nigella sativa oil, Tween 80, TWEEN 20. The *exvivo* evaluation was done and the penetration rate of vincristine in the formulation was analyzed in the Franz Diffusion cell. The result obtained shows a drug solubility of 70mg/ml in N.sativa oil and its water solubility is 0.03mg/ml. The *in vitro* permeation studies showed a 93.7%. The *ex vivo* evaluation proved that after 6 hours the release percentage vincristine were 86.7% respectively. Hence ME3 may be the most optimized preparation for the oral delivery of and the developed O/W microemulsion formulation was expected to be potential vehicles for the oral delivery of the drugs having low solubility, poor bioavailability. Finally, it can be concluded from the results of present study that Microemulsions improve the drug delivery, prolong the release, and improve the site specificity of the drug Vincristine. Microemulsions creates a new opportunity for the well-controlled drug delivery of a number of drugs that have a problem of administration by other routes

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