INTRODUCTION
The uncontrolled growth of cells and tissue can arises cancer, cancer was a one of the most distressing and life threading disease that serves date worldwide. Cancer like Brain tumors were an abnormal and uncontrolled growth of cells in brain. Modern colloidal nanoparticulate system was novel approach to overcome the problems of chemotherapy. Intranasal drug delivery was the promising strategies for direct deliver neurotherapeutic agent to nose to brain by passing the BBB via olfactory and trigeminal nerve pathways. Quercetin (QUR) (polyphenolic

ABSTRACT
Quercetin-flavonoid-polyphenolic has gained attention in prevention of brain cancer. The low permeability of Quercetin (QUR) across the blood-brain-barrier (BBB) leads to its insufficient delivery which in turns result in low therapeutic index. Therefore, developing a novel approaches enhancing the CNS delivery of QUR are required for the treatment of Cancer. The aim of this research work was to develop in Microemulsion (ME) loaded with QUR, for CNS targeting. Quercetin is a poorly water soluble anticancer drug, with oral bioavailability is about 4%. Microemulsion were fabricated by Spontaneous Emulsification technique. Oleic acid was used as oil. Tween 80 was employed as surfactant and Polyethylene glycol 400 was employed as co-surfactant. QUR loaded ME for intranasal delivery are considered as promising vehicle for its targeting to CNS to treat the brain cancer.

KEYWORDS
Intranasal delivery, Microemulsion, Brain targeting and Spontaneous emulsification technique.
compound) has potent antimetastatic and antiproliferative activity against brain tumors. It was important to suppression of nuclear factor-kB is responsible for tumor proliferation. QUR having a promising ability to inhibit angiogenesis, it is process for formation of new blood cell in blood vessel for tumor growth, QUR having ability to stop the new blood cell formation in blood vessels responsible for tumor growth and shows antiangiogenic activity. The goal of this study was formulate Microemulsion(ME) containing QUR for intranasal (nose to brain) delivery to central nervous system (CNS) for the treatment of brain tumor$^{1-3}$.

**MATERIAL AND METHODS**

**Materials**
Quercetin (QUR) was a gift from Loba Chemie Ltd. (Mumbai, India). Oleic acid, Tween 80 and polyethylene glycol 400 (PEG 400) were purchased from Loba Chemie Ltd. (Mumbai, India).

**FORMULATION OF MICROEMULSION (ME)**

**Selection of Excipients for formulation**
The solubility of Quercetin (QUR) in various oils (castor oil, oleic acid, ethyl oleate, soya oil, coconut oil, oleic acid and clove oil), surfactants (Tween 20 and Tween 80) and co-surfactant (polyethylene glycol 400, polyethylene glycol 200 and propylene glycol) was determined by using Screening technique$^4$.

**Preparation of Microemulsion (ME)**
Quercetin-Microemulsion (QUR-ME) were prepared by spontaneous emulsification technique (Low energy emulsification technique) by slowly pouring the oil, surfactant and co-surfactant mixture using Vortex mixer (Sphinix Ltd, India) into aqueous phase. QUR (100 mg/ml) was dissolved in mixture of Oleic acid (µl), Tween 80 (ml) and PEG 400 (ml) wasslowly added with stirring at 600rpm using magnetic stirrer and formulation composition was reported in Table No.1.

**PHYSICOCHEMICAL CHARACTERIZATION OF QUERCETIN LOADED MICROEMULSION (QUR-ME)**

**Photon correlation spectroscopy**
The mean droplet size (MDS) were determined by photon correlation spectroscopy (PCS) using a Malvern Zetasizer (Nano ZS 90, Malvern Ltd., Malvern, UK). The measurement using PCS is based on the light-scattering phenomena in which the statistical intensity fluctuations of the scattered light from the particles in the measuring cells are measured. Prior to the measurements, all samples were diluted with double-distilled water to produce a suitable scattering intensity the lights catterin g was monitored at 25$^\circ$C at a 90$^\circ$angle.$^5$

**Zeta Potential**
The ZP, reflecting the electric charge on the droplet surface and indicating the physical stability of colloidal systems, was measured by determining the electrophoretic mobility using the Malvern Zetasizer (Nano ZS 90, Malvern Ltd., and Malvern, UK). The measurements were performed following dilution in double-distilled water. It was measured using the Dip cell by applying a field strength of 20 V/cm and the average of the ZP was given from 30 runs.$^6$

**Drug Content**
The drug content of formulation (F5) was determined by UV spectrophotometric method. QUR from ME formulations was extracted by dissolving 1 ml of ME in methanol. QUR content in the Methanolic extract was analyzed spectrophotometrically (UV 1700, Shimadzu, Japan) at 257 nm, against the standard Methanolic solution of QUR.$^7$

**In vitro Drug permeation studies**
In vitro diffusion study of optimized ME was carried out by Franz diffusion cell having 2.0 cm diameter and 25 ml capacity. Dialysis membrane (Himedia) having molecular weight cut off range 12000 - 14000 kDa was used as diffusion membrane. Pieces of dialysis membrane were soaked in phosphate buffer saline (PBS) pH 6.4 for 24 h prior to experiment. Diffusion cell was filled with PBS pH 6.4 and dialysis membrane was mounted on cell. The temperature was maintained at 37$^\circ$C. After a pre-incubation time of 20 minutes, the ME equivalent to 10 µg of QUR was placed in the
donor chamber. Samples were periodically withdrawn from the receptor compartment for 4 hours and replaced with the same amount of fresh PBS, and assayed by a UV spectrophotometer at 257 nm.

**Histopathological Studies**

Histopathological studies were carried out using isolated sheep nasal mucosa. Three sheep nasal mucosa pieces (A, B and C) with uniform thickness were selected and mounted on Franz diffusion cells. A was treated with PBS (pH 6.4, Negative control, C with isopropyl alcohol (Positive control), and B was treated with drug (QUR) loaded ME respectively. After treatment for 8 hours, all the samples were washed properly with double distilled water, sectioned and stained with hematoxylin and eosin. The mucosa was dissected out, then subjected to histological studies to evaluate the toxicities of ME and photographed by optical microscope.

**RESULTS AND DISCUSSION**

**Preparation and characterization of Microemulsion**

The QUR-ME were prepared using spontaneous emulsification technique. For the preparation of oleic acid as a liquid lipid. Tween 80 were selected as a surfactant and Polyethylene glycol 400 as a cosurfactant a stabilizer, respectively.

**Photon correlation spectroscopy and Zeta Potential**

The droplet size (nm) and zeta potential (mV) of QUR-loaded ME (F5) was found to be 116.41 nm and -39.13 mV respectively.

**Drug Content**

The concentration of oil and surfactant: cosurfactant was important effect on drug content. The oil content (oleic acid) was increases, to increase drug content and the surfactant and co surfactant concentration (tween 80 + PEG 400) decreases to increase drug content. Because drug having maximum solubility in oil phase and drug content of optimized formulation (F5) was found to be 99.65 %.

**In vitro Drug permeation studies**

The release profile of QUR-loaded ME (F5) through the dialysis membrane in PBS (pH 6.4) was found to be 99.84 %. The release pattern of optimized ME appears to be fast release with negligible burst effect.

**Histopathological studies**

It is necessary to examine histological changes in nasal mucosa caused by formulations, if it is to be considered for practical use. Histological studies show negative control mucosa (normal nasal mucosa) and positive control mucosa stained with hematoxylin-eosin and the effect of formulation on sheep nasal mucosa, 8 hours after applying the formulations (Figure No.1). No change in mucosal structure was seen when treated with drug loaded ME (F5) as compared to the positive control. The section of mucosa treated with formulation QUR-ME showed no changes in nasal epithelium. There was no sign of remarkable destructive effect of formulations on the treated nasal mucosa.

**Table No.1: Compositions of QUR-ME formulations**

<table>
<thead>
<tr>
<th>S.No</th>
<th>Formulation batches</th>
<th>Con. of Oil (Oleic acid) (µl)</th>
<th>Con. of Surfactant (Twean 80) (ml)</th>
<th>Con. of Co-surfactant (PEG 400) (ml)</th>
<th>Particle size in (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F1</td>
<td>300</td>
<td>12.00</td>
<td>9</td>
<td>185.12</td>
</tr>
<tr>
<td>2</td>
<td>F2</td>
<td>300</td>
<td>12.00</td>
<td>10</td>
<td>155.95</td>
</tr>
<tr>
<td>3</td>
<td>F3</td>
<td>300</td>
<td>10.00</td>
<td>12</td>
<td>176.84</td>
</tr>
<tr>
<td>4</td>
<td>F4</td>
<td>300</td>
<td>9.50</td>
<td>15</td>
<td>254.29</td>
</tr>
<tr>
<td>5</td>
<td>F5 (op)</td>
<td>280</td>
<td>6.00</td>
<td>8</td>
<td>116.41</td>
</tr>
<tr>
<td>6</td>
<td>F6</td>
<td>350</td>
<td>12.00</td>
<td>9</td>
<td>187.25</td>
</tr>
<tr>
<td>7</td>
<td>F7</td>
<td>400</td>
<td>9.00</td>
<td>12</td>
<td>165.41</td>
</tr>
<tr>
<td>8</td>
<td>F8</td>
<td>365</td>
<td>12.00</td>
<td>10</td>
<td>178.25</td>
</tr>
</tbody>
</table>
CONCLUSION
QUR have various activities as it may be anticancer, antioxidant, anti-inflammatory drug lipophilic in nature having low oral Bioavailability (4%) is selected as candidate for the development of ME for its intranasal delivery to target the CNS. The result of present investigation shows that drug loaded QUR-ME for intranasal administration may be very a promising approach for delivering an anticancer agent in order to achieve CNS targeting for the treatment of brain tumor, in particular, for producing the cytotoxic effect. However, clinical benefits to the risk ratio of the formulation developed in this investigation will decide its values in the clinical practice for the treatment of brain tumor.

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CONFLICT OF INTEREST
We declare that we have no conflict of interest.

BIBLIOGRAPHY
6. Patel A R, Vavia P R. Preparation and in vivo evaluation of SMEDDS containing


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