A Review on Solid Lipid Nanoparticle of Artesunate And Mefloquine HCl For Malaria Treatment: A Novel Approach

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Abstract: Malaria may be quite common disease. Malaria may be a disease caused by a parasite. People suffering altogether age. In India around 2 Million of individuals suffer from Malaria. Sesquiterpine and Quinoline-methanol lactones are use to treat the malaria cause by the plasmodium falciparum parasite. Artesunate and Mefloquine HCl is highly effective and utilized in treatment of Malaria. Artesunate and Mefloquine HCl used for the great therapeutic effect and improve bio availability got to be prolong drug release. Solid Lipid Nanoparticles are solid colloidal particles starting from 1 to 100 nm in size, they contain micro molecular materials during which the active ingredients (drug or biologically active material) is dissolved, entrapped or encapsulated, or adsorbed, or attached. release of drug form nanoparticle are without dose dumping.

Keyword: Malaria, Artesunate, Mefloquine HCl, Solid Lipid Nanoparticle drug delivery, Hot Homogenization technique.

INTRODUCTION

INTRODUCTION TO MALARIA(1-4)

- Malaria may be a disease of the blood which will be fatal. It’s caused by the eukaryotic protists Plasmodium spp. The protists are spread to humans most ordinary through mosquitoes of the Anopheles.
- Malaria mainly caused by the one among protozoan parasites and it have mainly 4 types:
  1. Plasmodium Falciparum
  2. Plasmodium Vivax
  3. Plasmodium Ovale
  4. Plasmodium Malaria
- Malaria Affect Over 40% population of the planet.
- WHO Estimate That There Are 350-500 Million Cases Of Malaria World Wide.
- In India 2 million Cases And 1000 Deaths in a year.

SYMPTOMS OF MALARIA

- within the condition of Malaria Symptoms like, feel very sick, with a high fever and shaking chills, vomiting, headache, anemia, Nausea. Dry cough, Muscle pain, Fatigue, Chest or abdominal pain.
CAUSES OF MALARIA

- Malaria is caused by the Plasmodium parasite.
- The parasite are often spread to human through the bites of infected female anopheles mosquitos.
- Because the parasites that cause malaria affect red blood cells (RBC), people also can catch malaria from exposure to infected blood including:
  a. From mother to unborn child
  b. Through transfusion
  c. By sharing needles want to inject drug

DIAGNOSIS

- Rapid Diagnostic assay (Test)
- Clinical Diagnosis
- Microscopic Diagnosis
- Molecular Diagnosis
- Serology

Rapid Diagnostic assay (Test)

- When microscopy isn’t readily available, rapid diagnostic tests could also be used rather than blood smears. These tests detect malaria antigens during a sample of a patient's blood from finger and indicate a positive result by a color change on the testing strip in 2-15 minutes. This method is additionally called "dipstick" tests.

- Different rapid diagnostic tests are available. For instance, some rapid tests may detect all four common species (P. falciparum, P. vivax, P. ovale, P. malariae) but don’t distinguish between them. Others are combination tests which will detect all four common species and can identify P. falciparum specifically if it’s present. The sort of rapid test used is depends on the patient population and therefore the goals of providing a rapid test result for diagnosis.

Clinical Diagnosis

- This diagnosis is predicated on the patient’s symptoms and on physical findings at examination.
- Clinical findings should be every time approved by a laboratory test for malaria.
Microscopic Diagnosis

- It are often identified by examining under the microscope a drop of the patient’s blood, open up as a “blood smear” on a slide before to examination, the specimen is stained to offer the parasites a particular appearance. this system remains the gold standard for laboratory approving of malaria.

Molecular Diagnosis

- Parasite nucleic acids are finding by the “polymerase chain reaction” (PCR). Although this system could also be slightly more sensitive than smear microscopy, it’s of limited utility for the diagnosis of acutely patients within the standard healthcare setting. PCR results are often not available quickly enough to be useful in establishing the diagnosis of malaria infection. PCR is most useful for confirming the species of malarial parasite after the diagnosis has been authorize by either smear microscopy or RDT.

Serology

- Serology help to finding antibodies against malaria parasites, by the indirect ‘immunofluorescence’ (IFA) or ‘enzyme-linked immunosorbent assay’ (ELISA). Serology doesn’t detect current infection but rather measures past exposure.

EPIDEMIOLOGY:

- Malaria Affect Over 40% population of the planet.
- WHO Estimate That There Are 350-500 Million Cases Of Malaria World Wide.
- In India 2 million Cases And 1000 Deaths in a year.
- Consistent with WHO Report 2018:

<table>
<thead>
<tr>
<th>YEAR</th>
<th>TOTAL CASE</th>
<th>DEATH</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>210 MILLION</td>
<td>4,59,000</td>
</tr>
<tr>
<td>2015</td>
<td>211 MILLION</td>
<td>4,46,000</td>
</tr>
<tr>
<td>2016</td>
<td>216 MILLION</td>
<td>4,45,000</td>
</tr>
<tr>
<td>2017</td>
<td>219 MILLION</td>
<td>4,35,000</td>
</tr>
</tbody>
</table>
AVAILABLE MANAGEMENT:

1. Non-Pharmacological

2. Pharmacological

NON-PHARMACOLOGICAL MANAGEMENT

- Keeping mosquitoes from biting
- Sleep under insecticide-treated bed nets
- Use insectifuge
- Eat food containing higher level of iron. Example: beetroot, Spinach
- Wear long-sleeved clothing if out of door in the dark
Table no.:2: Management of Malaria

<table>
<thead>
<tr>
<th>Class</th>
<th>Example of medicines</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-Aminoquinoline</td>
<td>Chloroquine, Amodiaquine, Piperaquine</td>
</tr>
<tr>
<td>Quinoline-methano</td>
<td>Mefloquine HCl</td>
</tr>
<tr>
<td>Cinchona alkaloid</td>
<td>Quinine, Quinidine</td>
</tr>
<tr>
<td>Biguanides</td>
<td>Chloroguanide</td>
</tr>
<tr>
<td>Diaminopyrimidines</td>
<td>Pyrimethamine</td>
</tr>
<tr>
<td>8-Aminoquinolin</td>
<td>Primaquine, Bulaquine</td>
</tr>
<tr>
<td>Sulfonamide</td>
<td>Sulfadoxine</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Tetracycline, Doxycycline</td>
</tr>
<tr>
<td>Sesquiterpine lactones</td>
<td>Artesunate, Artemether, Arteether</td>
</tr>
<tr>
<td>Amino alcohol</td>
<td>Halofantrine, Lumefantrine</td>
</tr>
</tbody>
</table>

INTRODUCTION TO SOLID LIPID NANOPARTICLES(SLN)\(^{(5-10)}\)

- Solid lipid nanoparticles (SLNs) emerged in 1991 with the target to supply biocompatibility, storage stability and to stop the incorporated drug from degradation.
- SLNs, colloidal carriers of nanoscopic size (50–1000 nm), made from solid lipids (high melting fat matrix), are developed to overcome the weaknesses (e.g., polymer degradation, lack of an appropriate large scale production method, inferior stability, drug leakage and fusion, phospholipid degradation, high cost, and sterilization problems) of traditional colloidal carriers, like polymeric nanoparticles and liposomes.
- Solid Lipid Nanoparticles provide the various distinctive appearance related to the low toxicity, large surface, prolonged drug release, cellular uptake as correlated to traditional colloidal carriers also as capability to improve solubility and bioavailability of medicines.
- The discharge of drug from SLNs depends on matrix type and drug location within the formulation.
- The formulation of SLNs from biodegradable and biocompatible ingredients are ready to inbuilt both hydrophilic and lipophilic bioactives and thus stemming to be a various option for controlled and targeted drug delivery.
- The solid core of SLNs is hydrophobic with a monolayer coating of phospholipids and therefore the drug is typically dispersed or dissolved within the core.

INGREDIENTS USED IN THE FORMULATION OF SOLID LIPID NANOAPRTICLE

SLN formulation composed of internal phase and external phase. Internal phase contain drug +Lipid+Oleic Acid dissolved in desired solvent. And external phase contain water and Poloxamer 407.

1. LIPID: Lipid store the structure, transport and release of drug. Utilized in internal phase.
- Glycerol mono stearate (GMS)
- Bees Wax
- Stearic acid
- Cholesterol
- Cholesterol Butyrate

2. **SURFACTANT**: It provides stability and reduce the interfacial surface tension of the SLN. It utilized in the External phase.
   - Poloxamer 407
   - Tween 80
   - Lecithin

3. **SOLVENT**: Solvent are utilized in internal phase also as External phase.
   - Ethanol
   - Acetone
   - water

**METHOD OF PREPARATION:**

- Drug added in melted lipid (GMS)
- Melted lipid added in ethanol + oleic acid
- Dispersion of lipid phase in to aqueous phase
- Pre-emulsion using stirrer (1000 RPM)
- Hot oil in water nano emulsion
- Cooling to room temperature
- High pressure homogenation
- Solidification
- Drying
- Solid lipid nanoparticle

**Figures No.4 Method of Preparation**

**Evaluations Parameters of Solid Lipid Nanoparticles**(11-19):

- **Particle size**
  
  Particle size are calculated using optical microscope or an electron microscope. This is often a crucial step, because the size of the particles greatly affects the feel of the formulation and its stability.

- **Morphology and Surface topography**
  
  Morphology and surface topography, various techniques are used Scanning electron microscopy (SEM), transmission electron microscopy (TEM) etc.
Determination of % Entrapment Efficiency & % yield

The % Entrapment Efficiency & Production yield of the Solid Lipid Nanoparticle are often calculated consistent with the subsequent equation:

- % Entrapment Efficiency = actual drug content in SLN / Theoretical drug content x 100
- % Yield = Practical Yield / Theoretical Yield x 100

Dissolution Test:

In vitro release of Artesunate and Mefloquine HCl from solid lipid nanoparticles was evaluated by the dialysis bag diffusion technique. The release studies of solid lipid nanoparticles were performed in phosphate buffer (pH 7.4). The SLN was placed during a cellulose dialysis bag and sealed at both ends. The dialysis bag was immersed within the receptor compartment containing 50 mL of in phosphate buffer (pH 7.4), which was stirred at 100 rpm and maintained at 37 ± 0.5°C. The receptor compartment was covered to stop the evaporation of dissolution medium. Samples were withdrawn (5ml) at regular time intervals (1 hour), and therefore the same volume was replaced by fresh dissolution medium. The samples were analyzed employing a UV-visible spectrophotometer.

FORMULATION PROTOCOL:

First prepared Solid Lipid Nanoparticle of Artesunate and Mefloquine HCl by Hot Homogenization method then take like dose and prepared capsule. which is employed to improved drug release of ARTesunate and Mefloquine HCl.

STABILITY STUDIES

To measure the drug and formulation stability, stability studies were done consistent with ICH and WHO guidelines. Optimized formulation Solid Lipid Nanoparticle were kept within the humidity chamber maintained at 40°C and 75% RH for 1 months. The sample were analysed for the physical changes and % drug content, in vitro release profile and other stability indicating parameters after 15 days and 1 month.

Conclusion: Oral delivery of Solid Lipid Nanoparticle is novel approach. Artesunate and Mefloquine HCl having low solubility So, the drug resistance are going to be seen. Solid Lipid Nanoparticle drug delivery system provide prolong drug release by altering the particle size which provides good therapeutic effect against parasite without dose dumping. Solid Lipid Nanoparticle drug delivery have number of benefit which will provide the large scope in future for the delivery of drug topically also as orally with more efficacy and lower cost.
Reference:


