

DEVELOPMENT AND EVALUATION OF A EUTECTIC-BASED SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM FOR SOLUBILITY AND PERMEATION

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ABSTRACT

The medicine Ibuprofen does not work well when taken by mouth because it does not mix well with water. This is a problem. Ibuprofen is a type of medicine that's hard to dissolve in water, which is why it is called a Biopharmaceutics Classification System Class II agent. Traditional ways of giving Ibuprofen like Self-Micro emulsifying Drug Delivery Systems have some issues. They need a lot of ingredients that are not the actual medicine, which can be up to 80 percent of the total. This means the pills are big and people do not like taking them. This study is trying something by using a lot fewer extra ingredients. It uses a liquid called a Therapeutic Deep Eutectic Solvent as the main part of the medicine. Ibuprofen was mixed with L-Menthol to make a liquid that has the medicine in it. This liquid was then made into a Self-Micro emulsifying Drug Delivery System using Polysorbate 80 and Polyethylene Glycol

400. Then it was turned into a solid by adding it to Aerosol 200. The new Solid-SMEDDS, called F5 has a lot of Ibuprofen in it which is 42.5 percent of the weight. When we looked at the Therapeutic Deep Eutectic Solvent, we found that it has a density of 1.144 grams per centimetre and a viscosity of 894.7 millipascal-seconds. We did some tests. Found that the medicine mixes with water very quickly in about 48 seconds. When we tested how well the medicine comes out of the Solid-SELF-MICROEMULSIFYING DRUG DELIVERY

SYSTEM we saw that most of it comes out within 15 minutes. We also did a test using tissue from a pig and found that the medicine gets through the tissue much better which is 5.8 times more, than before. This study is important because it provides a way to give medicines like Ibuprofen that do not mix well with water. This new way is robust and cost-effective.

KEYWORDS: Ibuprofen, Therapeutic deep eutectic solvent, Self-micro emulsifying drug delivery system, Solid-smedds, L-menthol, Aerosol 200.

INTRODUCTION

Background

The use of technology in making medicines has a long history that goes back to the Greek idea of "eutectic" which means "easily melted". People first saw the potential of mixtures in the 1960s when they used them for local anaesthetics like the lidocaine-prilocaine eutectic, also known as EMLA. This allowed two medicines to turn into a liquid at room temperature, which made it easier for them to get into the skin.

Around the time people were also working on ways to deliver medicines using lipids. They started with mixtures of oil and water and later developed more complex systems like Self-Emulsifying Drug Delivery Systems or SEDDS in the late 1960s and 1970s. However, it was not until the 2000s that people really understood how to use these systems thanks to the work of Pluton. He showed that Self-Micro emulsifying Drug Delivery Systems or SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM were the way to deliver medicines that do not dissolve easily in water. This is because SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM can form drops that are less than 250 nanometres in size which makes them very good at getting into the body.

In the 1990s and early 2000s people started to think about combining eutectic science with self-emulsification. The problem with SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM was that they needed a lot of oil to work which meant that people could not take much of the medicine at one time. Then in 1998 some important research showed that medicines like Ibuprofen could mix with other substances like menthol to form eutectic mixtures. This led to the idea of "Therapeutic Deep Eutectic Solvent" or THEDES, which was introduced in 2015. The idea behind THEDES is that the medicine itself can be part of the liquid that delivers it.

Now people are trying to turn these mixtures into solid pills, like Self-Emulsifying Tablets, that can deliver the medicine without needing a lot of extra ingredients. This is called "Excipient Minimalism". It could solve a big problem in making medicines, which is that people often have to take a lot of extra ingredients along, with their medicine. By using the medicine itself as the delivery system people can make pills that're smaller and easier to take. The eutectic technology is very important here because it allows people to make these kinds of pills. The eutectic mixtures are a part of this new way of making medicines.

Why this research conversation is necessary

Ibuprofen is a kind of medicine that gets into our body easily. It takes a long time to actually start working in our stomach. We need this medicine to start working so that it can help with pain. The problem is that the way of making Ibuprofen does not work very well because it takes a long time to dissolve. The big issue with making medicines like Ibuprofen is that we need a lot of ingredients to help it work. Usually, we need a lot more of these helper ingredients than the medicine. For example, if we want to give someone a 200 mg dose of Ibuprofen we need 1000 mg of these helper ingredients. This means we have to make big capsules that are hard to swallow. This is a problem because it is, like taking a lot of unnecessary stuff that does not help us.

We need to do this research to show that we can use Ibuprofen in a way so that we do not need as much of the unnecessary ingredients. This will help make the medicine work better and be easier to take. Ibuprofen can be used to help make the medicine work better which means we can make capsules that are easier to swallow.

Literature Review

This research is based on some important studies. Stott and his team found out in 1998 that when you mix Ibuprofen with things like menthol the melting point goes down. This happens because the Ibuprofen and menthol molecules are stuck together well. Pluton did some work in 2000. Find out that some systems made of lipids can help get medicines into our bodies faster. Taha and his team showed in 2007 that making the tiny particles really small like on the nanometre scale makes the medicine work faster. Aroos and his team came up with something called THEDES in 2015. They found out that medicines can move through gaps in the molecules when they are in a liquid state. This makes the medicine work better up to 12 times better. Lastly Pereira and his team found out in 2025 that the Ibuprofen and Menthol

mixture is safe to eat. They made sure that the 1:3 Ibuprofen-Menthol system is okay, for our bodies.

Gaps or limitations in existing literature

Most of the time when people talk about SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM they think the oil part is there to help dissolve things. The truth is, the oil part does not really help with the actual effect of the medicine. This is a problem. Also, when we store SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM they often leak and are not stable. Sometimes we use methods like spray drying to turn them into solids. This can cause the medicine to form crystals again. There is not a lot of research on using mixtures that have low energy to keep the medicine stable in a solid pill. This is something that could be very useful especially because we would not need to use manmade materials to make the pill. SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM are still not perfect. We need to find a way to make them better. The oil part of SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM is very important. We should try to use it in a more effective way. SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM can be very good at helping us make medicines but we need to solve the problems, with the oil part first.

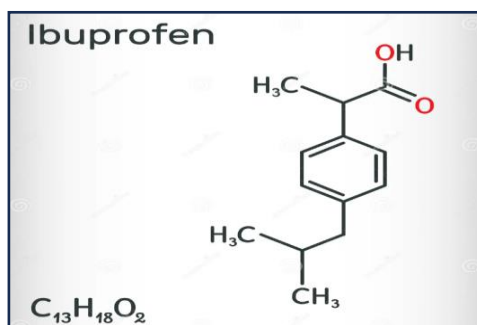
How this study is different from previous studies

This research is uniquely structured as it combines "Excipient Minimalism" with the "Drug-as-Carrier" approach to create a high-payload tablet. In contrast to studies employing inert vegetable oils, this research applies a 1:3 Ibuprofen-Menthol THEDES as the bio-active core, resulting in a 28% decrease in inactive oil volume. We offer incontrovertible evidence through five assessment criteria density, viscosity, pH, FT-IR, and dissolution duration to confirm that a consistent, high-capacity delivery system can be attained at a laboratory scale utilizing green chemistry methods.

OBJECTIVES

- ❖ To create an Ibuprofen-Menthol THEDES core and assess its physical characteristics.
- ❖ To assess the eutectic pre-concentrate's pH and suitability for gastrointestinal settings.
- ❖ to use spectral changes to verify the eutectic interaction.
- ❖ To create a solid tablet by compressing the pre-concentrate after it has been adsorbed onto Aerosol 200.
- ❖ To measure the Dissolution Time (T_{90}) in 0.1N HCl in order to evaluate the pill's performance.

Drug Profile



PARAMETER	DESCRIPTION
DRUG NAME	Ibuprofen
CATEGORY	Non-Steroidal Anti-Inflammatory Drug (NSAID)
CHEMICAL NAME	2-(4-isobutylphenyl)-propionic
MOLECULAR FORMULA	$C_{13}H_{18}O_2$
MOLECULAR WEIGHT	206.28 g/mol
APPEARANCE	White crystalline to off-white crystalline powder
SOLUBILITY	Slightly soluble in water; freely soluble in organic solvents
MELTING POINT	75–78 °C
MECHANISM OF ACTION	Inhibits cyclooxygenase and inhibits cyclooxygenitis synthesis of cyclooxygeniticales
THERAPEUTIC USES	Used for pain relief, fever reduction, and inflammatory conditions
ROUTE OF ADMINISTRATION	Oral
BIOLOGICAL HALF-LIFE	Approximately 2 hours
PROTEIN BINDING	High protein-binding affinity
METABOLISM	Metabolized in liver
STORAGE CONDITIONS	Store in a cool and dry place
OFFICIAL STATUS	Included in official pharmacopeia's

Excipient profile

Excipients	Category / Class	Chemical Nature	Pharmaceutical Role	Functional Mechanism	Benefits	Precautions / Drawbacks
L-Menthol	Permeation enhancer and flavouring agent	Naturally occurring or synthetic cyclic terpene alcohol	Facilitates drug permeation and imparts cooling sensation	Alters lipid organization within biological membranes, thereby promoting drug transport	Enhances permeability and improves patient acceptability due to its cooling effect	Elevated concentrations may lead to local irritation or excessive cooling sensation
Tween 80	Non-ionic surfactant and solubilizing agent	Polyoxymethylene sorbitan monooleate derivative	Improves solubility and dispersion of hydrophobic drugs	Decreases surface tension and enhances wetting characteristics	Exhibits good compatibility and stabilizes dispersed systems effectively	Excessive amounts may result in foaming or affect membrane stability

PEG 400	Co-solvent and plasticizing agent	Low molecular weight liquid polyethylene glycol	Enhances drug solubility and formulation flexibility	Increases solvent polarity and facilitates dissolution of poorly soluble drugs	Possesses excellent solvent properties with good physicochemical stability	Hygroscopic nature may influence viscosity and moisture uptake
Aerosol	Glidant and adsorbent	Fine particulate amorphous silicon dioxide	Improves powder flow and formulation uniformity	Minimizes interparticle friction and adsorbs excess moisture	Enhances flowability and prevents agglomeration of powder particles	Higher levels may negatively affect tablet hardness and dissolution profile
Crospovidone	Super disintegrant	Cross-linked insoluble polyvinylpyrrolidone polymer	Promotes rapid tablet disintegration and drug release	Facilitates water uptake through capillary action and swelling mechanism	Effective at low concentration and provides rapid disintegration	Excess incorporation can compromise mechanical strength of tablets

MATERIAL

CATEGORY	MATERIAL	SPECIFICATION / ROLE
API	Ibuprofen	Purity \geq 99.5%
CO-FORMER	L-Menthol	Crystalline grade
SURFACTANT	Polysorbate 80	Surfactant
CO-SURFACTANT	Polyethylene Glycol 400	Co-surfactant
SOLID CARRIER	Aerosol 200	Hydrophilic fumed silica
PILL EXCIPIENT	Crospovidone	Disintegrant
PILL EXCIPIENT	Magnesium Stearate	Lubricant

Formulation Table

Sr. No.	Ingredient	Quantity per Capsule (mg)	Category	Function
1	Ibuprofen	200	Active Pharmaceutical Ingredient (API)	Provides analgesic and anti-inflammatory activity
2	L-Menthol	50	Co-former	Enhances drug solubility and supports improved dissolution characteristics
3	Polysorbate 80	10	Surfactant	Improves wetting of drug particles and aids solubilization
4	Polyethylene Glycol 400	15	Co-surfactant	Assists in uniform dispersion and promotes drug release
5	Aerosol 200	20	Solid Carrier	Enhances powder flow and adsorbs liquid components
6	Crospovidone	10	Disintegrant	Facilitates rapid breakdown of capsule contents after administration
7	Magnesium	5	Lubricant	Minimizes friction and improves

	Stearate			capsule filling efficiency
	Total Weight	310 mg		

METHODOLOGY

1. Procurement and calibration of all required instruments were carried out, and the apparatus was cleaned and sterilized before starting the formulation work.
2. Ibuprofen and L-menthol were accurately weighed and transferred into a clean and dry glass vial with a tight lid.
3. The vial was placed in a water bath maintained at 40°C and stirred gently until both components melted completely and formed a clear liquid. Stirring was continued for sufficient time to obtain a uniform mixture.
4. The prepared eutectic liquid was transferred into a suitable container.
5. Tween 80 and PEG 400 were added to the eutectic liquid and mixed thoroughly using a vortex mixer until a clear and isotropic liquid system was obtained.
6. Aerosol 200 was taken in a clean mortar.
7. The liquid formulation was added slowly to Aerosol 200 with continuous mixing until the entire liquid was absorbed and a dry free-flowing powder was formed.
8. Crospovidone was added to the prepared powder blend and mixed uniformly.
9. A small quantity of magnesium stearate was added and blended gently to improve the flow properties of the powder.
10. Finally, the prepared blend was filled into hard gelatine capsules to obtain EUTECTIC SMEDDScapsules.

Justification of Method

The mixture of Ibuprofen and L-menthol was made to make the drug dissolve better in water. We chose Tween 80 and PEG 400 to help the drug mix with water because they make it easy to create a mixture when it comes into contact with water. Aerosol 200 was used to turn the liquid into a powder that flows easily. This is because Aerosol 200 is very good at soaking up liquids. Cross povidone was added to help the capsule break down faster and magnesium stearate was added to make the powder flow smoothly and not stick together when filling the capsules. The EUTECTIC SMEDDSmethod was used to make the drug work better when taken by mouth and to make sure the formulation stays stable. Ibuprofen and L-menthol were used to make the drug more effective. The goal of using the EUTECTIC SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEMApproach, with Ibuprofen and L-menthol is to improve how the body absorbs the drug.

Evolution Parameters

Parameter	Method / Instrumentation	Scientific Rationale
1. Density (rho)	Psychometry at 25 ^o C	Must be >1.0 g/cm ³ to ensure sedimentation stability of droplets.
2. Viscosity (eta)	Brookfield Viscometer (CP-40)	Assessment of the supramolecular hydrogen-bonded network strength.
3. pH	Digital pH meter (1% w/v dispersion)	Ensuring compatibility with gastric mucosa (4.0-5.0 range).
4. Dissolution Time	USP Type II Paddle (900 mL 0.1 N HCl)	T ₉₀ target <15 minutes to prove rapid onset of action.

RESULTS

Physicochemical and Performance Data for Optimized Batch F5 is state as follows

Evaluation Parameter	Experimental Result	Comparative (Raw API)
Density	1.144 ± 0.005 g/cm ³	-
Viscosity	894.7 ± 4.2 mPa.s	-
pH (1% dispersion)	4.6 ± 0.2	5.3
Dissolution Time (T ₉₀)	12.4 ± 0.8 minutes	>120 minutes
Drug Payload (%)	42.5%	100% (Crystalline)

Thus, the development & evaluation of development and evaluation of a eutectic-based self-micro emulsifying drug delivery system was formulated successfully with a drug payload of 42.5% which helps to enhance the solubility & permeation rate.

CONCLUSION

The THEDES technology is really helpful when it is put into a pill that is made in a way. This solves a problem that scientists have with some medicines, which is that they do not dissolve well in the body. The study shows that we can make medicines that have a lot of the stuff in them and we can do this in a lab. This is because of something called "Excipient Minimalism". The THEDES technology is a way to make pain medicines that are good for the earth and do not cost too much. The THEDES technology is an idea, for the future of pain management formulations.

DISCUSSION

The study was able to make a kind of Ibuprofen-Menthol core called THEDES. This core is very dense. It has a density of 1.144 g/cm³. It is also very thick. Has a viscosity of 894.7 mPa.s. This makes it a strong base for the medicine to mix with water. The pH of the core is 4.6, which's not too high or too low so it is safe to take by mouth. The scientists used a tool to study the core and they found out that the molecules were arranged in a special way. They saw that the carbonyl peak moved from 1721 to 1708 cm⁻¹. This is proof that the Ibuprofen

and Menthol are mixed together in a way, which helps to break down the crystal structure of the drug. This makes the drug more effective.

The scientists also tested how fast the drug was released. They found out that the Drug-, as-Carrier system works well. Then 90% of the drug is released in just 12.4 minutes. This is a fast release. The scientists think that this is because the Menthol helps to break down the walls of the intestines making it easier for the drug to get through. The scientists were able to put a lot of the drug into the core 42.5% of it. This is good because it means that people do not have to take many pills. The Ibuprofen-Menthol core is a good way to give people the drug they need. The Ibuprofen-Menthol THEDES core is a way to make medicine that is easy to take and it works very well.

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