# A Novel Microparticle for Antimicrobial Activity

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***Abstract*: The current study concern with the preparation and evaluation of microparticle using HPMC and Ethylcellulose as polymer in the view of effectiveness, and easy of availability, cost effectiveness with sulphamethoxazole as model drug. Sulphamethoxazole is an active anti-bacterial drug having biological half-life of 8-10 hours and 86%-98% bioavailability and licensed for the treatment bacterial infection Microparticle of sulphamethoxazole were prepared using HPMC & EC by solvent evaporation technique. Compatibility study was carried out by using FTIR at the range of 4000 to 400 cm-1 shows no significant change in the characteristic peaks of sulphamethoxazole and excipients in all the formulation, which indicates the compatibility of sulphamethoxazole with excipients. The prepared microspheres were analysed for particle size, Micromeritic properties, % yield, % drug entrapment efficiency, in-vitro drug release studies, and antimicrobial activity and stability studies. spherical shape and size range of 100µm to 200µm. In-vitro drug release shows decreases as concentration of HPMC increases. We conclude that, microparticle offer a practical and suitable approach to prepare controlled Microparticles thus obtained were found to white colour and free flowing. Micromeritic studies of the prepared formulations are found within the prescribed limits and indicated good flow property. The Scanning Electron Microscopy (SEM) studies inferred the release of sulphamethoxazole with HPMC and EC as rate controlling agent to enhance bioavailability and reduction in dose frequency as well as patient compatibility.***

***Keywords*: Sulphamethoxazole, microparticle antibacterial, HPMC, EC and controlled release**

**Introduction:**

**MICROPARTICLES:** Topical drug administration is the most preferable route for taking medications. However, their short circulating half-life and restricted absorption via a defined segment of intestine limits the therapeutic potential of many drugs. Such a pharmacokinetic limitation leads in many cases to frequent dosing of medication to achieve therapeutic effect. This results in pill burden and consequently, patient complains. Rational approach to enhance bioavailability and improve pharmacokinetic and pharmacodynamic profile is to release the drug in a controlled manner and site-specific manner. (Bhowmik D. et al 2012)

Microparticles are a type of drug delivery systems where the particle size ranges from one micron (one thousandth of a mm) to few mm. This microencapsulation technology allows protection of drug from the environment, stabilization of sensitive drug substances, elimination of incompatibilities, or masking of unpleasant taste. Hence, they play an important role as drug delivery systems aiming at improved bioavailability of conventional drugs and minimizing side effect. (Pawan Kumar B. 2011) Microparticulate drug delivery system is one of the processes to provide the sustained & controlled delivery of drug to long periods of time. They are small particles of solids or small droplets of liquids surrounded by walls of natural & synthetic polymer films of varying thickness & degree of permeability acting as a release rate controlling substance & have a diameter upto the range of 0.1µm-200µm. Initially use of albumin microspheres in drug delivery system was suggested by Kramer in 1974. In 1997, Java Krishna and Catha proposed the use of microspheres as sustained release vehicles. There are also reports about using haemoglobin as natural biodegradable carriers for drugs for Microparticulate administration. Microparticles have been proved to be an ideal way of preparing sustained and controlled release dosage forms. They are also a beneficial way of delivering APIs which are pharmacologically active but are difficult to deliver due to limited solubility in water. In such drugs the attainment of high Cmax, Tmax, and Area under the curve is problematic. Thus, a need exists for immediate release products containing these agents. Microsphere-based formulations can be formulated to provide a constant drug concentration in the blood or to target drugs to specific cells or organs. (Pawan Kumar B. 2011)

1.1. MORPHOLOGY OF MICROPARITCLE Microencapsulation is a technology used to entrap solids, liquids, or gases inside a polymeric matrix or shell. Microparticles are particulate dispersions or solid particles. Two general micro-morphologies of Microparticles can be distinguished microcapsules and microspheres.

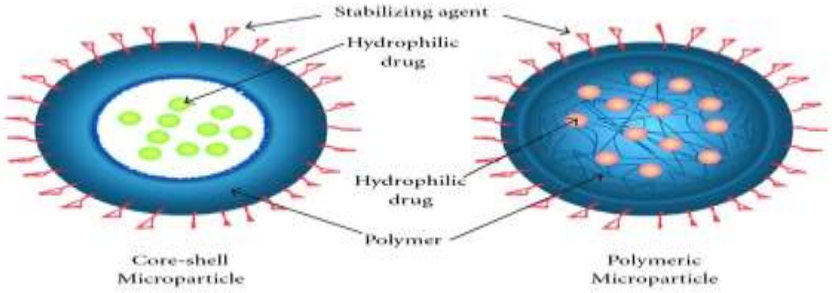



Fig: 1.1 structure of microparticle

**1.1.2. Advantage of microparticle:**

(1) Effective delivery of agents which are insoluble or sparingly soluble in water
(2) The technique provides the way for improving taste of an active agent.
(3) They increased the bioavailability of drugs.
(4) The formulation of Microparticles also provides the method of targeting the drug delivery to specific sites.
(5) The Microparticles hold great potential in reducing the dosage frequency & toxicity of various drugs.
(6) Microparticles in the form of microcapsules can also be used as carrier for drugs & vaccines as diagnostic agents & in surgical procedures.
(7) They provide the sustained release formulation with lower dose of drug to maintain plasma concentration & improved patient compliance.

**1.1.3. Disadvantages:**

1. The costs of the materials and processing of the controlled release preparation, which may be higher than those of standard formulations.
2. They are affected on the environment.
3. They are affected of polymer additives such as plasticizers, stabilizers, antioxidants and fillers.
4. Reproducibility is less.
5. Process conditions like change in temperature, pH, solvent addition, and evaporation/agitation may influence the stability of core particles to been capsulated.
6. The environmental impact of the degradation products of the polymer matrix produced in hydrolysis, oxidation, solar radiation or biological response to heat.

**1.2. Material used for microparticle:**

The coating material can be selected from a wide variety of natural and Synthetic polymers depending on the core material to be encapsulated and the desired characteristics.

**1. Natural or synthetic hydrophilic colloids**

These are large molecules that are soluble or dispersible in aqueous solutions. Here the capsule wall presents a good barrier to oily and hydrophobic materials, but it is usually a poor barrier to hydrophilic substances
Examples: Amylodextrin, Amylopectin, cellulose derivatives, cellulose acetate PVP, PVA, Shellac etc.

**2. Biocompatible polymer**

It includes poly (lactic) acid, Natural polymers Albumin Chitin Starch The bioavailability enhancers used are lysophosphatidyl choline.

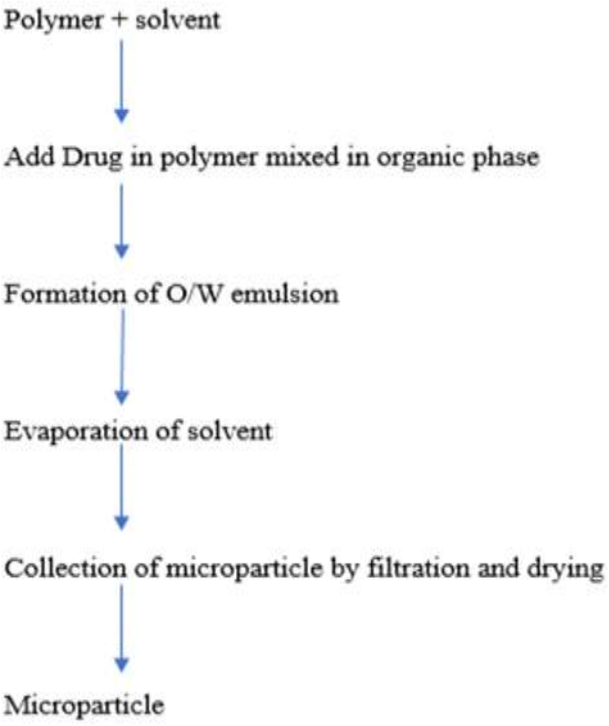
**3. Biodegradable polymer**

Biodegradable polymers have ability to degrade in the body naturally offer enormous advantages over conventional drug delivery systems. Some of the materials that are currently being used for controlled drug delivery include Poly methyl methacrylate, PVA, poly acrylamide, PEG, polylactic acid, poly glycolic acid.

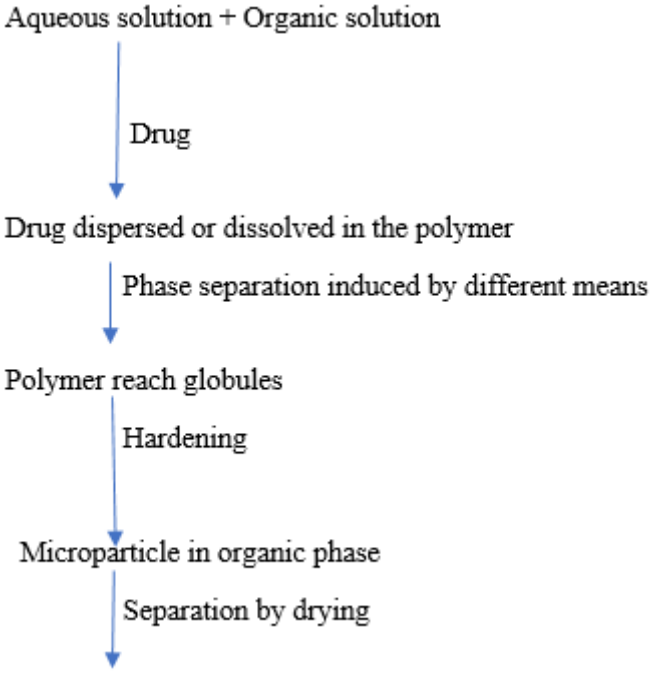
**1.3. Some of the methods include formulation of microparticle: -**

1. Emulsion–solvent evaporation (o/w, w/o, w/o/w).
2. Phase separation (non solvent addition and solvent partitioning).
3. Interfacial polymerization.
4. Spray drying.
5. Emulsion extraction process.
6. Jet milling technique.
7. Fluidization & solvent precipitation method.

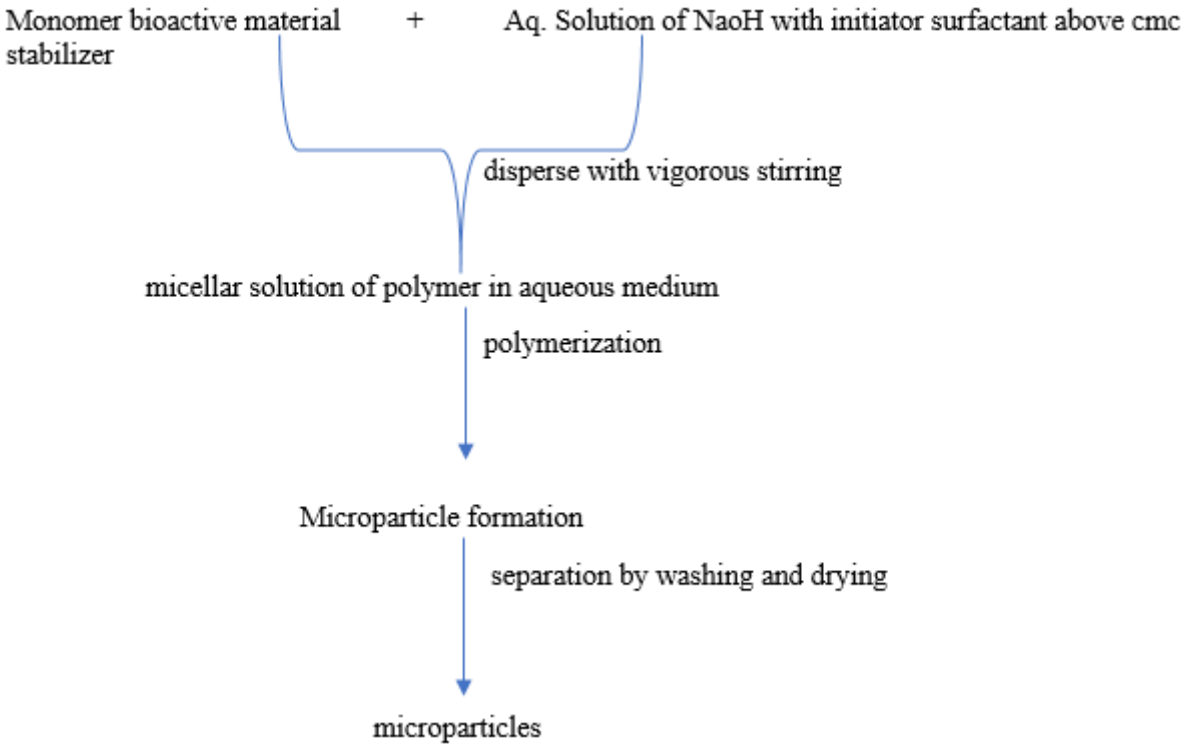
**1. 3.1. Emulsion–solvent evaporation (o/w, w/o, w/o/w).**




**1.3.2. Phase Separation**



**1.3.3. Interfacial polymerization**




**1.4. Applications of microparticles.**

1. Application of microcapsules include pharmaceutical and biotechnology products, cosmetics, diagnostic aids.
2. These microcapsules are important in providing sustained and controlled release, improving drug stability, vaporization of volatile oils, protecting from moisture/light/oxidation–sensitive drugs.
3. Amoxicillin, ampicillin, bacampicillin, cephalexin, cephradine, chloramphenicol, clarithromycin, erythromycin etc antibiotics are encapsulated.
4. PH triggered micro particles have been used to deliver drugs by various means ex-by IV injection, intra dermal injection, rectally, orally, intra vaginally, inhalationally, mursoual delivery etc.
5. They are also used for administering. An antigenic of a pathogen or a tumour.
6. The micro particles are useful in transfecting cells & gene therapy.

**1.5. Antimicrobial:**

Antibiotics are the substances produced by microorganisms, which suppress the growth or kill other microorganisms at very low concentrations antimicrobial drugs can be classified in many ways according to their chemical structure, mechanism of action, types of organisms, spectrum of activity, type of action, source of origin.

**Table no: 1. Classification of antibiotics:**

| | |
|---|---|
| **Penicillin's** | **1. Natural: - Penicillin G, Penicillin-V 2. Penicillinase Resistant: - Methicillin, Nafcillin, Oxacillin and other. 3. Aminopenicillins: - Ampicillin** |
| **Fluoroquinolones** | First generation: - nalidixic acid, Norfloxacin, Ofloxacin, Ciprofloxacin, Pefloxacin. Second generation: - Levofloxacin, Moxifloxacin, Lomefloxacin, Gemifloxacin, Sparfloxacin, Prulifloxacin |
| **Aminoglycosides** | Streptomycin, Gentamycin, Kanamycin, Tobramycin, Amikacin, Sisomicin, Netilmicin. |
| **Monobactams** | Aztreonam |
| **Carbapenems** | Imipenem, Meropenem, Faropenem, Doripenem |
| **Macrolides** | Azithromycin, Clarithromycin, Dirithromycin, Erythromycin, Clindamycin, Roxythromycin. |

**2. DRUG PROFILE**

**Sulphamethoxazole**.

Synonyms – Gantanol.

- Chemical formula - $C_{10}H_{11}N_3O_3S$
- Molecular weight – 253.28
- Structure

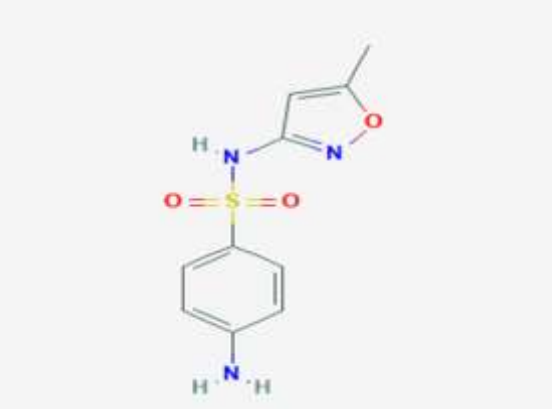


Fig: 2. Structure of sulphamethoxazole

**Description: Sulphamethoxazole** is an isoxazole (1, 2-oxazole) compound having a methyl substituent at the 5-position and 4-aminobenzenesulfonamido group at the 3-position. It has a role as an antibacterial agent, an anti-infective agent.
Sulfamethoxazole is a bacteriostatic sulphonamide antibiotic that interferes with folic acid synthesis in susceptible bacteria. It is generally given in combination with [trimethoprim] which inhibits a sequential step in bacterial folic acid synthesis - these agents work synergistically to block two consecutive steps in the biosynthesis of nucleic acids and proteins which are necessary for bacterial growth and division, and using them in conjunction helps to slow the development of bacterial resistance. In this combination, sulfamethoxazole is useful for the treatment of a variety of bacteria

**Physical description**
Colour – white crystalline powder
Odour – odourless
Taste: metallic
► Pharmacology Sulphamethoxazole is a bacteriostatic sulphonamide antibiotic that inhibits a critical step in bacterial folate synthesis. It is generally given in combination with [trimethoprim], a dihydrofolate reductase inhibitor, which inhibits the reduction of dihydrofolic acid to tetrahydrofolic. Studies have shown that bacterial resistance develops more slowly with the combination of the two drugs than with either trimethoprim or sulfamethoxazole alone, as together they inhibit sequential steps in the bacterial folate synthesis pathway. Sulphonamides, including sulfamethoxazole, have been implicated in hypersensitivity reactions - these agents should be discontinued at the first sign of a developing rash, as this may signal the start of a more severe reaction such as StevensJohnson syndrome or toxic epidermal necrolysis. Sulfamethoxazole treatment may contribute to folate deficiency and should therefore be used with caution in patients at a higher risk of developing a deficiency. Homolysis has been observed in patients with glucose-6-phosphate dehydrogenase deficiency that are using sulfamethoxazole/trimethoprim.

**2.1. Mechanism action of sulphamethoxazole:**

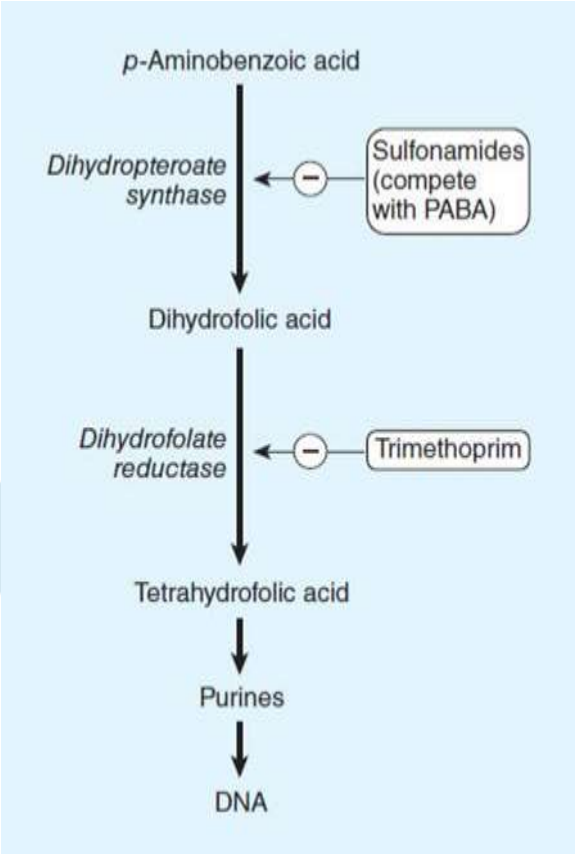



Fig: no. 3 flow chart of mechanism action of sulphamethoxazole.

**3.1. Preparation of the Microparticles:**

sulphamethoxazole Microparticles were prepared by solvent evaporation technique. different ratios of HPMC and ethyl cellulose combination were dissolve in 8.5 ml acetone separately and dispersed by using a magnetic stirrer .the core material sulphamethoxazole was added to the polymer solution and mixed for 15 minute ,followed by magnesium stearate (100mg) and then mixed thoroughly .the resulting solution was added in a thin stream to a mixture of 90 ml light liquid paraffin and 10 ml n-hexane containing in a 250 ml beaker while stirring at 700 rpm using a mechanical stirrer . stirring was continued for 3 hrs. until the acetone evaporated completely. the Microparticles formed were filtered using Whatman no.1 filter paper. The residue was washed 4-5 time with 50ml portion of n- hexane. The product was then dried at room temperature for 24 hours.

**4.1. Result and discussion**

**4.1.1. Preparation of stock solution**

I. Standard calibration curve of sulphamethoxazole

II. **Preparation of 70% ethanol**: take 72.16ml of pure ethanol and dissolve it with 27.84 ml of distilled water to get 70% ethanol.

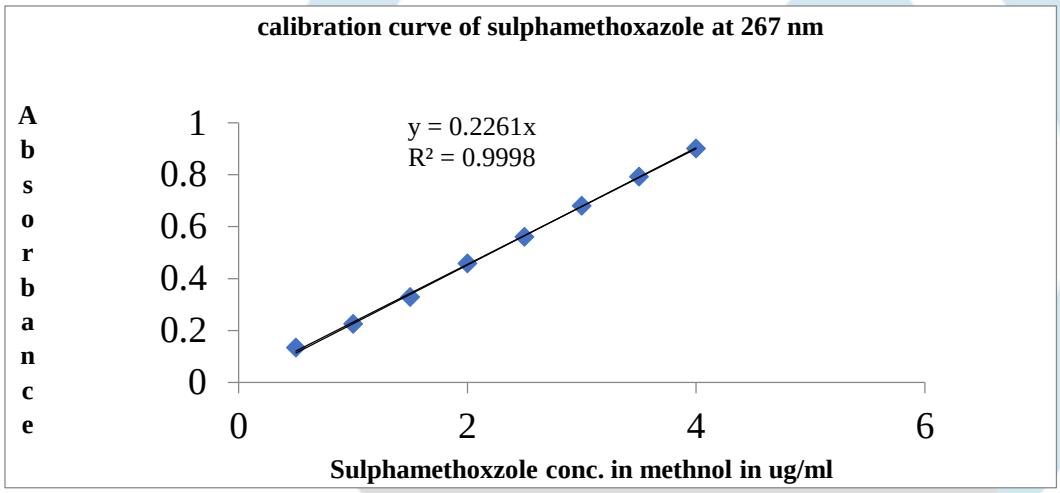
III. **Preparation of stock solution:** weight accurately 25mg of sulphamethoxazole. Then put it into 50ml volumetric flask and dissolved with 15ml (70%)) ethanol as a solvent and the volume was made up to mark with 0.1N NaOH to achieve the conc.500µg/ml. After that the above solution pipette out 5ml each into a 100ml volumetric flask and dilute with 70% ethanol so that obtained conc. of 25µg/ml

IV. **Absorption of sulphamethoxazole:** Pipette out of 1ml on working solution then transferred to a 25ml of volumetric flask and dilute with 0.1N HCl to get the conc. of 1µg/ml and further taken of the way 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0. Observe the lambda max absorbance at 257-267nm.

**CALIBRATION CURVE OF SULPHAMETHOXAZOLE:** Measured the absorbance of the above prepared standard solution at 267 nm. Plotted a graph of concentration (in µg/ml) on X axis and absorbance (in nm) on Y axis. (Fazel s. et al 2006.)

**Table no: 2. conc. And absorbance of sulphamethoxazole**

| S. No | Concentration (µg/ml) | Absorbance |
|---|---|---|
| 1 | 0.5 | 0.134 |
| 2 | 1.0 | 0.279 |
| 3 | 1.5 | 0.394 |
| 4 | 2.0 | 0.521 |
| 5 | 2.5 | 0.668 |
| 6 | 3.0 | 0.751 |
| 7 | 3.5 | 0.861 |
| 8 | 4.0 | 0.987 |




**4.1.2. Determination of λmax in phosphate buffer (pH 5.5):** The determination of the maximum absorption spectrum of sulphamethoxazole is at a concentration of 6.45mcg/ml and Determination of maximum absorption spectrum is measured at wavelength 200–400 nm. The maximum absorption spectrum of sulphamethoxazole can see at in 267 nm. (Muchlisyam et al 2019)

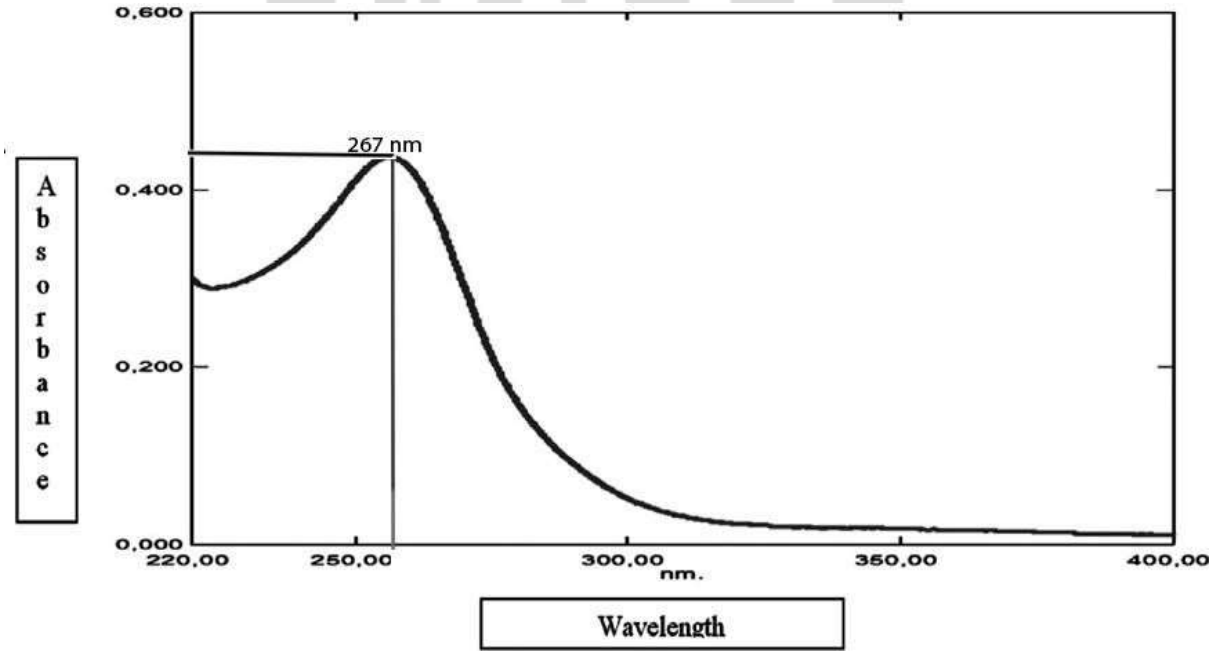



Fig: 4. λmax graph of sulphamethoxazole

**4.2. PRE-FORMULATION STUDIES**

**Organoleptic properties**

| Batch No | Bulk Density (g/ml) | Tapped Density(g/ml) |
|---|---|---|
| F1 | 0.2435 | 0.2918 |
| F2 | 0.2378 | 0.2878 |
| F3 | 0.2641 | 0.3241 |
| F4 | 0.2401 | 0.3010 |

These tests were performed as procedure given, Preformulation part. The results are illustrated in table no.3. (Raja sekharan T. et al 2009)

**Table no: 3. organoleptic properties of sulphamethoxazole powder**

| **Test** | **Specifications/limits** | **Observations** |
|---|---|---|
| Color | White to off white | White powder |
| Odour | Odourless | Odourless |
| Taste | Metallic | Metallic |

**Angle of repose:** It was determined as per procedure and the value found to 19.79.

**Bulk density and tapped density:** of sulphamethoxazole powder found to 0.48 ± 0.01, 0.67 ± 0.01

**Powder compressibility and Hausner:** It was determined as per procedure and it was found to 9.05± 0.01 mm and 1.22

**Melting point:** It was determined as per procedure and result was found to 169 $^{O}$C

**pH of the drug:** It was determined as per procedure and result found to 5.3

**Solubility:** It was determined as per procedure and result was found to

**Table no: 4 solubility study of sulphamethoxazole**

| S. no | Solubility | observation |
|---|---|---|
| 1 | Water | Practically insoluble |
| 2 | Methanol | Freely soluble |
| 3 | Ethanol | Sparingly soluble |
| 4 | Acetone | Freely soluble |

**4.3. EVALUATION OF MICROPARTICLE: -**

The angle of repose, bulk density, tapped density, cars index and Hausner ratio of the microparticle of sulphamethoxazole were performed as per the Preformulation procedure and the obtained resulted were illusered on the table no. 9,10, and 11. (Desai Ujjwal et al 2014)

**Table no:5. Angle of repose of microparticle**

| Batch No | Angle of Repose (°) |
|---|---|
| F1 | 24°24′ |
| F2 | 24°09′ |
| F3 | 27°62′ |

**Bulk densities and tapped density:** The bulk densities of formulation were found to in the range of 0.2371 to 0.2641 g/cm3 and the tapped density were found to be between in the range of 0.2742 to 0.2918 g/cm3. This result pointed that the drug has good packaging capacity. (Prashant et al 2018)

**Table no: 6. Bulk density and tapped density of microparticle formulation**

**Carr's Index and Hausner ratio:** The value Carr's Index of all formulation of sulphamethoxazole microparticle are ranged between the 13.53 to 20.23 % and that range of the carr's index show the good flow properties of the formulation as well as the Hausner ratio ranged to be found to 1.15 to1.25 which show passable flow properties

**Table no: 7. Carr's Index and Hausner ratio of microparticle**

| Batch No | Carr's Index (%) (Td-Bd/ Td*100) | Hausner Ratio (Td/Vd) |
|---|---|---|
| F1 | 16.55 | 1.19 |
| F2 | 17.37 | 1.21 |
| F3 | 18.51 | 1.22 |
| F4 | 20.23 | 1.25 |

**4.4. PERCENTAGE YIELD DRUG ENTRAPMENT EFFICIENCY OF SULPHAMETHOXAZOLE MICROPARTICLE:** Drug Loading and Drug Entrapment: The values of % of drug loading and % of entrapment efficiency are shown in Table 12,13. As the polymer concentration was increased the % of drug loading increase and % of entrapment efficiency was also decreased due to increase in the viscosity of the solution. This can be attributed to the permeation characteristics of each polymer used, that could facilitate the diffusion of part of entrapped drug to the surrounding medium during preparation of microparticle. (El-say et al 2016)

**Table no: 8. Drug Loading**

| S. No | Formulation Code | Weight of Drug Content (mg) | Actual weight of drug in microparticle | % Drug Loading |
|---|---|---|---|---|
| 1. | F1 | 250 | 90 | 36 |
| 2. | F2 | 250 | 112.457 | 44.98 |
| 3. | F3 | 250 | 105.96 | 42.38 |
| 4. | F4 | 250 | 106.99 | 42.79 |

**Table no: 9. Drug Entrapment efficacy**

| S. No | Formulation Code | Weight of Drug Content (mg) | Weight of polymer with drug | Actual drug weight in microparticle | Entrapment efficacy |
|---|---|---|---|---|---|
| 1. | F1 | 250 | 500 | 90 | 18.02 |
| 2. | F2 | 250 | 550 | 112.457 | 20.45 |
| 3. | F3 | 250 | 600 | 105.96 | 17.66 |
| 4. | F4 | 250 | 650 | 106.99 | 16.46 |

**Percentage yield:** Percentage yield of different formulation F1 to F4 were calculated and the yield was found to be 62%, 61.8%, 63.33%, and 64.61%, % respectively. The percentage practical yield slightly increases as the polymer ratio increased. (El-say et al 2016.

**Table no: 10. Percentage yield**

| S. No | Formulation Code | Wt. Of drug with polymer mixture (mg) | Wt. Of microparticle (mg) | % yield= wt. Of microparticle/ wt. of drug and polymer mixture * 100 |
|---|---|---|---|---|
| 1. | F1 | 500 | 310 | 62 |
| 2. | F2 | 550 | 340 | 61.8 |
| 3. | F3 | 600 | 380 | 63.33 |
| 4. | F4 | 650 | 420 | 64.61 |

**Particle Size Analysis**: The average particle size for the formulation F1 to F4 containing hydroxypropyl methyl cellulose was found to be in range from1.0± 0.001µm to 3.2±0.001µm. With increase in polymers concentration in the microparticle from F1 to F4, the particle size of microparticle increases respectively. This is because the viscosity of the polymer solution increases with increasing polymer concentration, which in turn decreases the stirring efficiency. (Chen W. 2016)

**Table no: 11. Particle Size**

| S. No | Formulation code | Average particle size (µm) |
|---|---|---|
| 1. | F1 | 1.0±0.001 µm |
| 2. | F2 | 1.6±0.002 µm |
| 3. | F3 | 2.0±0.001 µm |
| 4. | F4 | 2.2±0.001 µm |

**4.5. Scanning electron microscope:**

The determination of shape and surface morphology was done by scanning electron microscope (High resolution field emission scanning electron microscope) ZEISS model. SEM analysis of the samples revealed that all microparticle prepared were Hexagonal and cuboidal in shape. The microparticle of sulphamethoxazole with HPMC, Hexagonal and slightly aggregated particles. Scanning electron photomicrographs of the formulations are shown in fig. No10 (Zaini Erizal et al 2020)

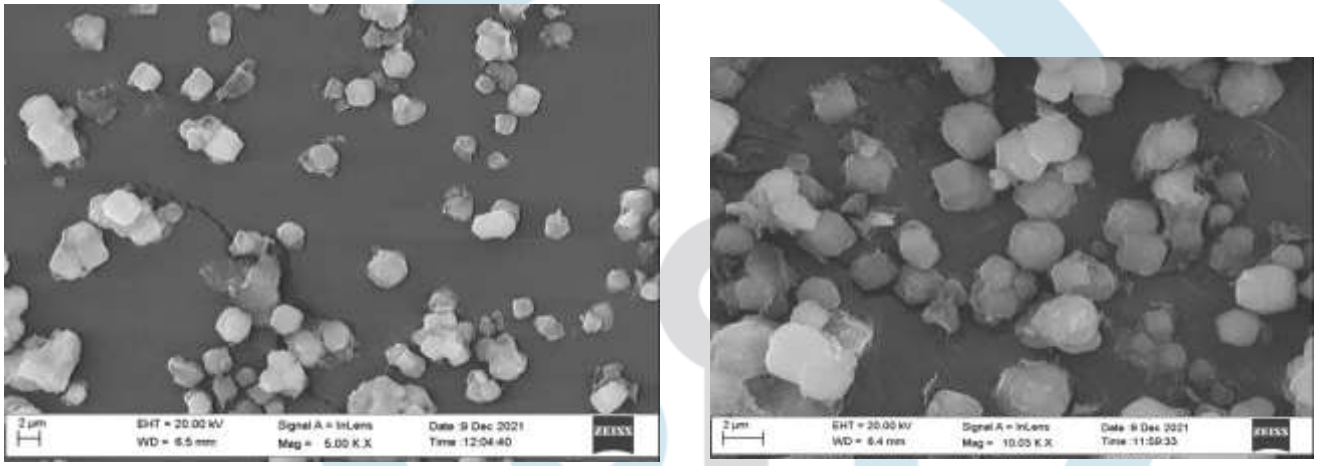
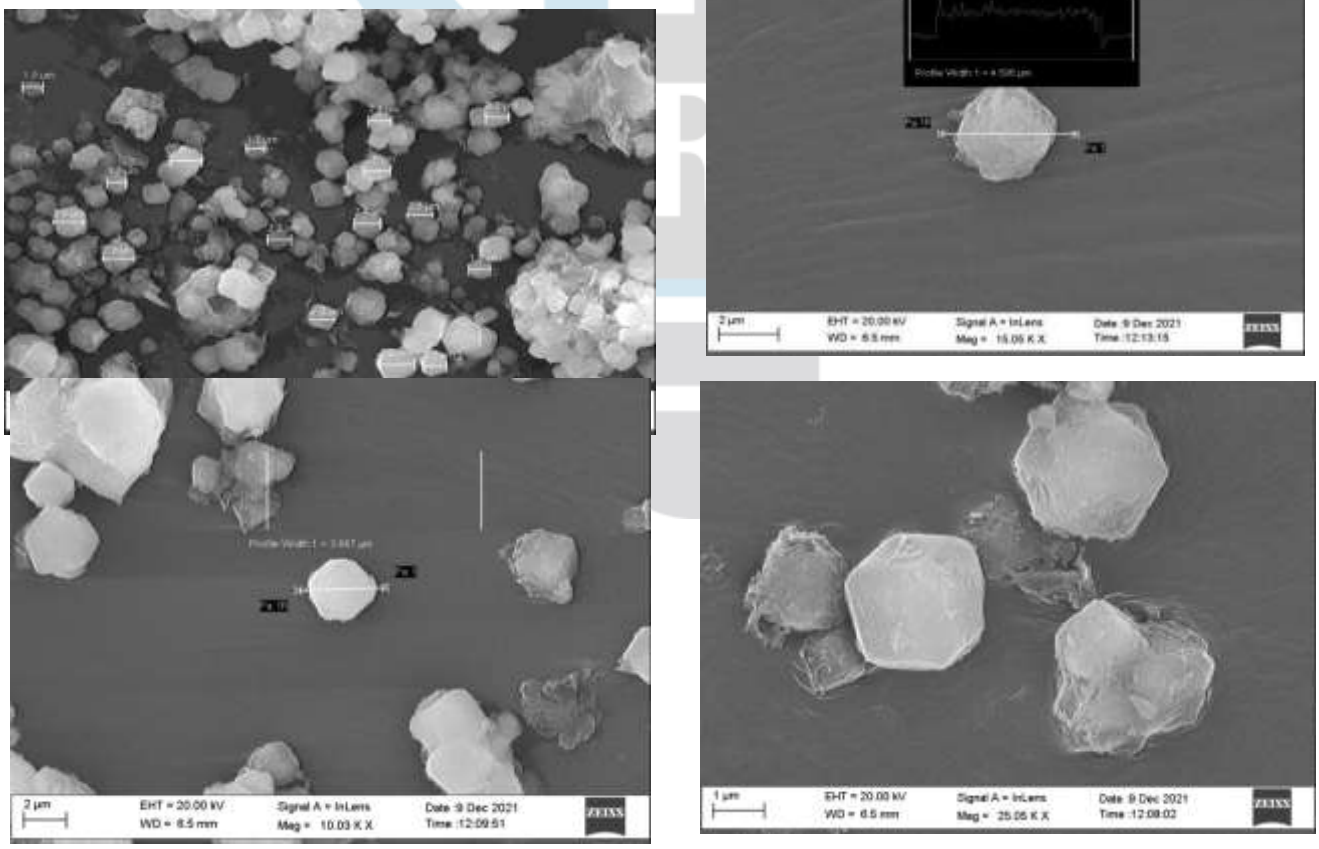


**Fig no.4. SEM analysis of microparticle of F2 formulation**



**4.6. Invitro drug release:** Dissolution studies of sulphamethoxazole microparticle were carried out using a USP dissolution apparatus Type II at pH 5.5 phosphate buffer solutions was used as the dissolution medium. The in-vitro drug release data of formulations are shown in Table. No.16,17,18, and 19. The cumulative percentage drug release after 3 hours was found to be in the range of 8.697,13.05,20.548,26.308,33.897,36.806,43.797 and 50.248 for the formulations F1, the cumulative drug release significantly decreased with increase in polymer concentration. The increased density of the polymer matrix at higher concentrations results in an increased diffusion path length. This may decrease the overall drug release from the polymer matrix. Furthermore, smaller microparticle are formed at a lower polymer concentration and have a larger surface area exposed to dissolution medium, giving rise to faster drug release. (Sari Retno et al 2019).

**Table no: 12. Release of F1 formulation microparticles.**

| s.no | Time in min. | % of drug release in mg F1 | % of drug release in mg F2 | % of drug release in mg F3 | % of drug release in mg F4 |
|---|---|---|---|---|---|
| 1. | 0 | 0 | 0 | 0 | 0 |
| 2. | 15 | 8.697 | 4.197 | 3.297 | 3.896 |
| 3. | 30 | 13.05 | 12.898 | 14.400 | 12.6 |
| 4. | 45 | 20.548 | 18.000 | 20.248 | 18.9 |
| 5. | 60 | 26.308 | 24.596 | 22.348 | 21.740 |
| 6. | 90 | 33.897 | 26.548 | 30.100 | 25.790 |
| 7. | 120 | 36.806 | 29.248 | 33.400 | 30.880 |
| 8. | 150 | 43.797 | 35.396 | 35.390 | 32.680 |
| 9. | 180 | 50.248 | 38.700 | 37.944 | 36.144 |

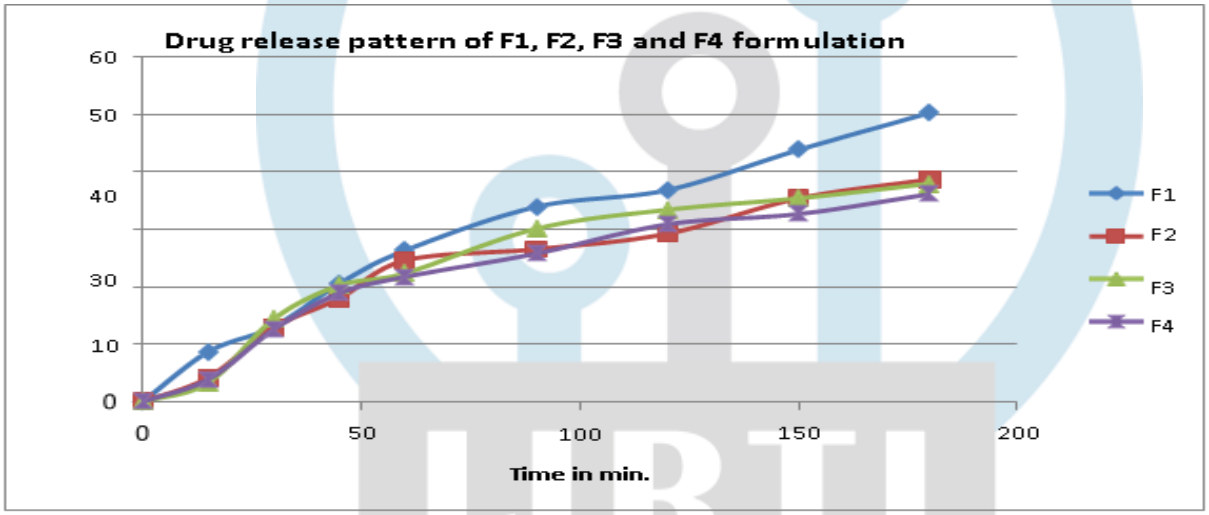



**Fig no: 5. Drug release pattern of F1, F2, F3 and F4 formulation**

**4.7. Stability study**

Stability study of microparticle were performed by using F1 formulation for 4 week and those were measured at different time intervals during stress condition and the stability% are shown in below table no 20. (Hardenia Shiv Shankar et al 2011)

**Table no:13. Stability study: stability study of F1 formulation of sulphamethoxazole microparticle (40ºc ±2 ºc / 75% ± 5% RH)**

| S. NO | Days | % R.D.C. (30oc) | % R.D.C. (40oc) |
|---|---|---|---|
| 1. | 1 week | 100.00 + 0.00 | 100.00 + 0.00 |
| 2. | 2 weeks | 99.97 + 0.024 | 99.95 + 0.018 |
| 3. | 3 weeks | 99.84 + 0.032 | 99.81 + 0.026 |
| 4. | 4 weeks | 99.63 + 0.045 | 99.54 + 0.031 |

**4.8. Antimicrobial activity of F2 formulation of sulphamethoxazole microparticle:** Sulphamethoxazole microparticles were evaluated for their in vitro antimicrobial activities against the pathogenic bacteria and their inhibition activities are shown on. (Anmar Hameed jabbir 2016)

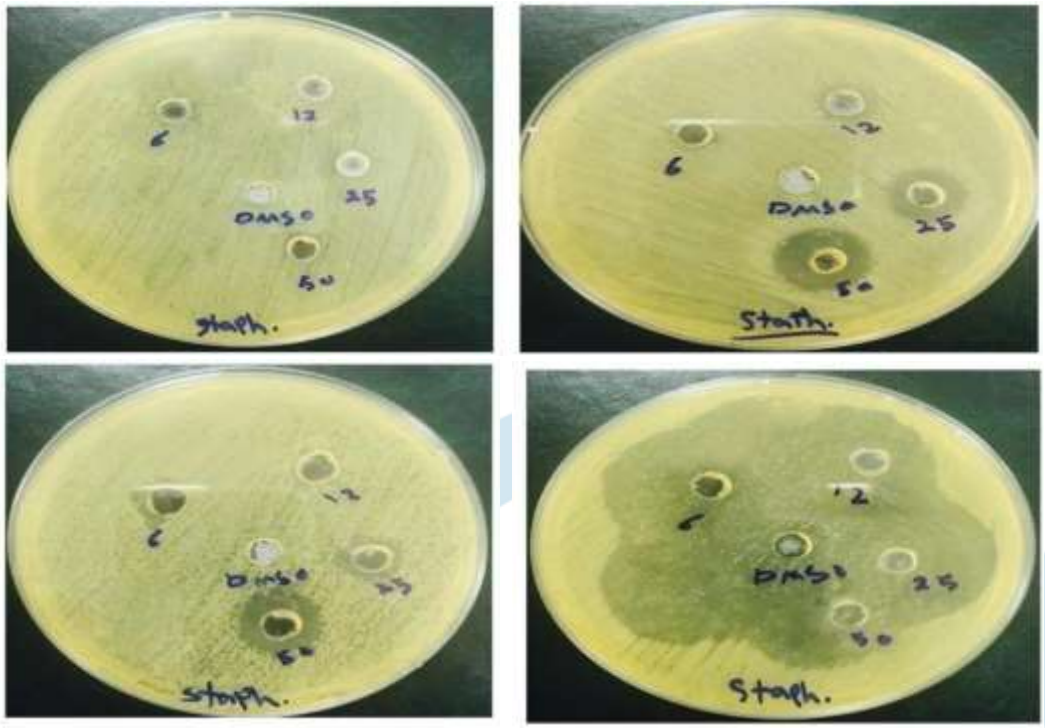



**Fig no: Fig: 16. Antimicrobial activity of sulphamethoxazole le by using staphylococcus Bactria.**
**(a) First week activity. (b) second week activity. (c) third week activity. (d) fourth week activity**

**CONCLUSION:**

The surface morphology of the prepared microparticle was studied using scanning electron microscopy. The prepared microparticles also characterized by FTIR spectroscopy to find out any chemical interaction between sulphamethoxazole and polymers used. The prepared microparticles were evaluated for particle size, percentage yield, drug incorporation efficiency, Micromeritic properties (like bulk density, tapped density, Hausner ratio, angle of repose, compressibility index), Invitro drug release study, as described in chapter 4.5. The results indicated that the significant effect was observed of increased polymer concentration, on said parameters in each case. The details of results are given in chapter 4. The mean particle size of the microparticles significantly increased with increase in polymer concentration. Micromeritic study suggested excellent flow properties of prepared microparticle. The Invitro release was in the following order F1>F2>F3>F4.

The results of the present study on "A novel microparticle for antimicrobial activity" reveals following conclusions:

Microparticles of sulphamethoxazole can be successfully prepared by using ethyl Cellulose and HPMC as matrix material and magnesium sulphate as the porous Material.

The percent yield of all microparticle formulation was more than 64% suggesting that the methods used for drug entrapment was effective. The percent yield was significantly increased as the amount of polymer was increased in each preparation method.

The in-vitro release was more than 50 % after 3 hours indicated satisfactory performance of proposed formulations. The percent increased significantly as the amount of polymer was increased in each preparation method.

The mean particle size of microparticles was in the range of 1-2. µm depending upon the concentration of polymer used. The particle size increased significantly as the amount of polymer increased.

The flow properties of all the prepared microparticles were good as indicated by low Angle of repose ($\theta < 19.79$) and low compressibility index. The good flow properties Suggested that the microparticle produced were non-aggregated.

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