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RESEARCH ARTICLE

Formulation and Characterization of Nanoparticles Loaded with Cefadroxil

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ABSTRACT:
Nanotechnology encompass a range of techniques rather than a single discipline and stretches across the whole spectrum of science, touching medicines, physics, engineering and chemistry. Targeted delivery of ingredients to a particular cell type or receptor. Capable of heat triggered local release. Nanoparticles are made up of non-biodegradable polymers such as methylmethacrylate or it can also be made from biodegradable polymers such as alkylcyano acrylate and albumin. Numerous methods exist for the manufacture of preparation of nanoparticles, allowing extensive modulation of their structure, composition and physiochemical properties. Formulation of nanoparticles of Cefadroxil using Albumin and Eudragit RL 100 in the ratios 1:1 and 1:2. Characterization of nanoparticles and invitro release of drugs has been carried out. In vitro release studies of each polymer was evaluated the synthetic polymer was exhibiting more extended release than natural polymer and the proportion have its influence in extending the release rate of the drug. The half-life of drug using Albumin loaded is 4hr and using Eudragit RL 100 is 4-5hr. Anti-bacterial studies has been done to confirm the anti-bacterial activity.

KEYWORDS: Nanoparticles, Albumin, Eudragit RL 100, antibacterial.

INTRODUCTION:

Nanotechnology is the science of the extremely tiny. It involves the study and use of materials on an unimaginably small scale. Nano refers to a nanometre (nm). [(1)]One nanometre millionth of a millimetre or about one eighty thousandth the width of a human hair. Nanotechnology encompass a range of techniques rather than a single discipline and stretches across the whole spectrum of science, touching medicines, physics, engineering and chemistry.

Nanotechnology in Medicines:

Nanotechnology involve the identification of precise targets (cells and receptors) related to specific clinical conditions and choice of the appropriate Nano carriers to achieve the required responses while minimizing the side effects.[(2)]

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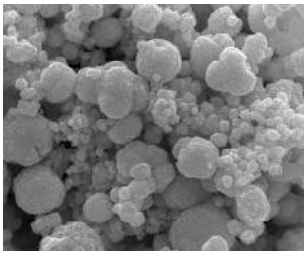
Nanoparticles:

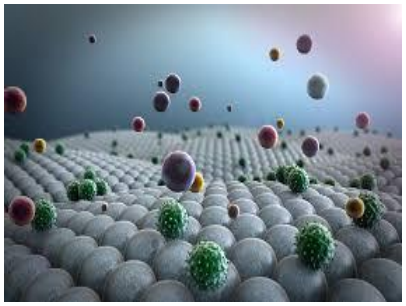
Nanoparticles consists of macromolecular materials and can be used therapeutically for e.g. as adjuvant in vaccines or drug carriers in which the active principle (drug or bioavailability active material) is dissolved, entrapped or encapsulated and which the active principle is absorbed or attached.

Carriers Used in The Preparation of Nanoparticles:

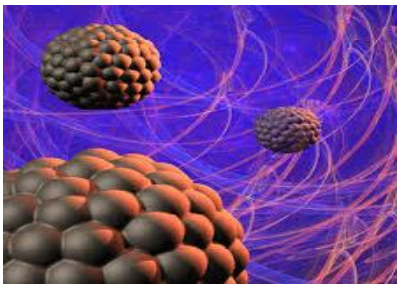
The polymers used for the preparation of nanoparticles are either Amphiphilic macromolecules, obtained from natural sources, hydrophilic polymers or synthesized chemically.[(3)]

Characterization:

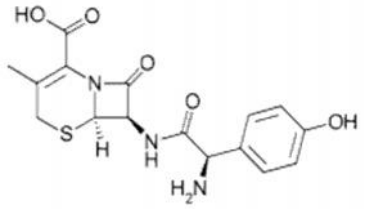




Physiological methods for the characterization of nanoparticles are listed. Size is their most prominent feature, although other parameters, such as density, molecular weight, and crystallinity, influence nanoparticles release and degeneration properties, whereas surface charge, hydrophilicity and hydrophobicity significantly influence the interaction with the biological environment after administration to humans and animals and the resulting body distribution.[4,5,6]



INTRODUCTION ABOUT THE DRUG



These are a group of semi-synthetic antibiotic derived from "Cephalosporin –C" obtained from fingers "Cephalosporin". They are chemically related to penicillin. Cefadroxil is a broad-spectrum antibiotic of the cephalosporin type, effective in Gram-positiveand Gram-negative bacterial infections. It is a bactericidal antibiotic.

HALF LIFE: About 1-4 hour to 2-6 hour.

POLYMER PROFILE EUDRAGIT RL 100:
EUDRAGIT RL 100 is a copolymer of ethyl acrylate, methyl methacrylate and a low content of methacrylic acid ester with quaternary ammonium groups. The ammonium groups are present as salts and make the polymers permeable. Physical properties: It is a solid substance in form of colourless, clear to cloudy granules with a faint amine-like odour.

SOLUBILITY:

Table - 1

Type	AA	DCM	SEA	1N HCl	1N NaOH	PE	W
Eudragit RL 100	**S**	**S**	**S**	-	-	**I**	**I**

Where, AA= Acetone and Alcohols ; DCM= Di-chloromethane; SEA=Solvent Ethyl acetate; PE= Petroleum ether; W= Water; S= soluble; I= Insoluble or immiscible ; Alcohols including ethanol, methanol and propane 2 – ol.

MATERIALS AND METHODS:

Preparation of Cefadroxil Loaded Egg Albumin and Eudragit Nanoparticles:

Drug polymer ratio

Drug	:	polymer
1	:	1
1	:	2

Table - 2

S.No	Egg albumin nanoparticles	Eudragitnano particles
1	Cefadroxil	Cefadroxil
2	Albumin	Eudragit RL-100
3	10% HCl	Chloroform
4	5% NaOH	Gelatin
5	Acetone	Cooling centrifuge
6	4% Gluteraldehyde	Ultra Sonicator
7	Electronic single pan balance	Electronic single pan balance
8	pH meter	Vacuum drier
9	U.V. Visible Spectrophotometer	
10	Centrifuge	
11	Vacuum Drier	
12	Ultra Sonicator	

Procedure of egg albumin nanoparticles:

Nanoparticles were prepared by pH – coaservation method. 100mg of egg albumin was taken in 50ml beaker and mixed with 100mg of the drug solution in 10% HCl then adjusted the pH to 8. The solution was sonicated by Ultra Sonicator with 5% NaOH solution and acetone was added drop wise from a syringe until the solution become turbid. The formed particles are

cross linked by adding 100ml of 4% gluteraldehyde solution was sonicated continuously for 3 hours at room temperature.[7,8] After the cross linking stage, the egg albumin nanoparticles were centrifuged at 5000rpm for 30 minutes. After centrifuging the supernatant liquid was removed and the suspension was washed till it is free from acetone and then finally dried in a vacuum drier.[9]

Procedure of eudragit nanoparticles:

The drug Cefadroxil polymer Eudragit are accurately weighed and Cefadroxil was dissolved in water and Eudragit in chloroform. The two solutions are mixed and were emulsified by ultrasonification for 45 minutes at 15°C in an aqueous 0.5% W/W Gelatin solution.[9] The solvent evaporate during 45 minutes at 40°C under continuous sonification. The nanoparticles formed is separated by Fractional centrifugation using a cooling centrifuge. The solution was centrifuged for about 15,000 rpm at 20°C for 15 minute. The supernatant fluid was discarded. The product was dried in vacuum drier.

Standard curve of Cefadroxil has been estimated. Dissolution study has been carried out.

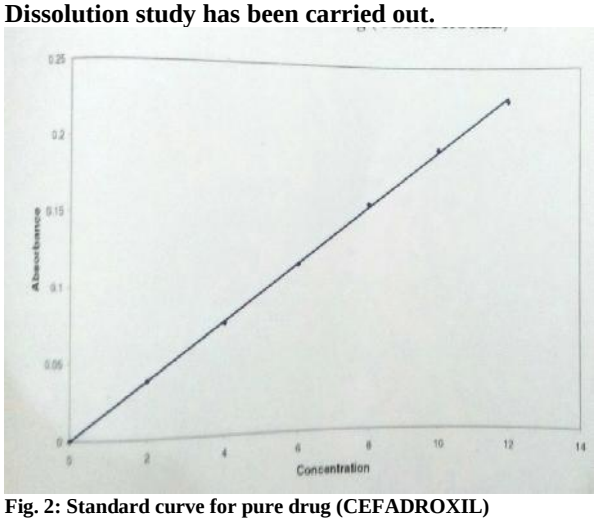


Fig. 2: Standard curve for pure drug (CEFADROXIL)

Characterization

Drug Content Analysis:

The drug content for Albumin loaded nanoparticles was analysed by adding 100ml of 1% hydrochloric acid solution with 0.1 ml of formulated nanoparticle and kept at room temperature for 24 hrs. [10, 11,12, 13]

Drug loaded capacity =

$$\frac{\text{mg of drug bound by total amount of nanoparticles}}{\text{Total amount of applied drug (mg)}}$$

The method adopted to carry out the invitro antibacterial activity was filter paper disc and media used was Muehler Hinton Agar.

RESULTS AND DISCUSSIONS:

Shorter biological half-life may necessities. Repeated administration of drug, which may reduce patient convenience and compliance Cephalosporin group of antibiotics, cefadroxil exhibits a shorter biological half-life, with wide anti-bacterial activity which required frequent doses, in order to reduce the toxicity and frequency Cefadroxil nanoparticle was formulated. Nanoparticle carrier of Cefadroxil was formulated using a natural polymer Albumin and a synthetic polymer Eudragit in the ratio 1:1 and 1:2. Two methods were adopted for the formulation one method adopted was the cross-linking method by using Eudragit polymer and the other being the pH-coacervation method using albumin as carrier drug polymer ratio and the cross link was presented.

Table – 3 Synthetic and Drug Polymer Ratio

S.NO	Batch Code	Amount of drug	Amount of polymer	Conc of cross-links agent	Drug-polymer ratio
1	A1	100mg	100mg	4% Gluteraldehyde	1:1
2	A2	200mg	200mg	4% Gluteraldehyde	1:2
3	E1	100mg	100mg	0.5% w/w Gelatin	1:1
4	E2	200mg	200mg	0.5% w/w Gelatin	1:2

A1 = 1:1; E1 = 1:1; A2 = 1:2; E2 = 1:2

Table – 4 Absorbance and Concentration

S.No	Formulations	Absorbance	Concentration %
1	A1	0.96	50.52%
2	A2	0.89	46.84%
3	E1	0.90	47.37%
4	E2	0.93	48.94%

A1 = 1:1 ; E1 = 1:1; A2 = 1:2; E2 = 1:2

Table – 5 Drug release rate of pure drug (CEFADROXIL)

Time in hrs	Absorbance	Conc mg/ml	Conc mg/900ml	% Release
30 min	0.5428	28.57	25.72	25.72
1hr	0.7486	39.4	35.46	35.46
2hr	1.1315	59.55	53.6	53.6
3hr	1.5276	80.4	72.36	72.36
4hr	1.9025	100.13	90.12	90.12

Table – 6 Drug release rate of ALBUMIN loaded Nano particles (Ratio 1:1)

Time in hrs	Absorbance	Conc mg/ml	Conc mg/900 ml	% Release
1hr	0.6126	32.24	29.02	29.02
2hr	0.788	41.47	37.33	37.33
3hr	0.9611	50.59	45.53	45.53
4hr	1.1136	58.61	52.75	52.75
5hr	1.3874	73.02	65.72	65.72
6hr	1.5436	81.24	73.12	73.12
7hr	1.7955	94.5	85.05	85.05

Table – 7 Drug release rate of ALBUMIN loaded Nano particles (Ratio 1:2)

Time in hrs	Absorbance	Conc mg/ml	Conc mg/900 ml	% Release
1hr	0.488	25.69	23.12	23.12
2hr	0.6232	33.06	29.76	29.76
3hr	0.8148	42.88	38.6	38.6
4hr	1.001	52.68	47.42	47.42
5hr	1.273	67	60.3	60.3
6hr	1.4197	74.72	67.25	67.25
7hr	1.6747	88.14	79.33	79.33
8hr	1.8698	98.41	88.57	88.57

Table – 8 Drug release rate of EUDRAGIT loaded Nano particles (Ratio 1:1)

Time in hrs	Absorbance	Conc mg/ml	Conc mg/900 ml	% Release
1hr	0.3614	19.02	17.12	17.12
2hr	0.4678	24.62	22.16	22.16
3hr	0.5979	31.46	28.32	28.32
4hr	0.7653	40.28	36.25	36.25
5hr	0.9204	48.44	43.6	43.6
6hr	1.1214	59.02	53.12	53.12
7hr	1.2947	68.14	61.33	61.33
8hr	1.4682	77.28	69.55	69.55
9hr	1.6331	85.96	77.36	77.36

Table – 9 Drug release rate of EUDRAGIT loaded Nano particles (Ratio 1:2)

Time in hrs	Absorbance	Conc mg/ml	Conc mg/900 ml	% Release
1hr	0.2603	13.7	12.33	12.33
2hr	0.3884	20.44	18.4	18.4
3hr	0.487	25.63	23.07	23.07
4hr	0.6365	33.5	30.15	30.15
5hr	0.7963	41.91	37.72	37.72
6hr	0.9578	50.41	45.37	45.37
7hr	1.1159	58.73	52.86	52.86
8hr	1.278	67.27	60.54	60.54
9hr	1.4836	78.07	70.26	70.26

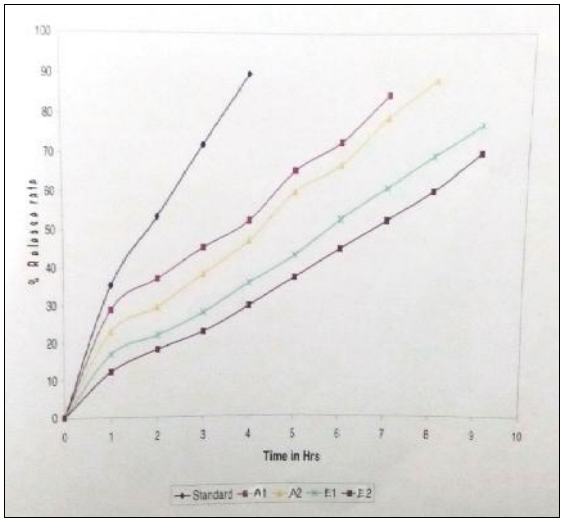


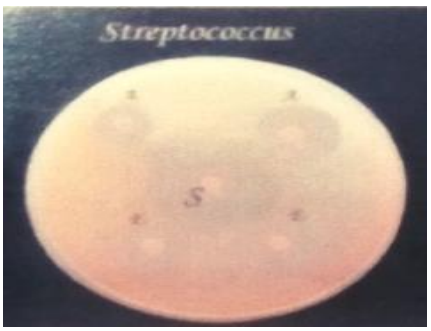
Fig. 3 Comparison and release rate of pure drug and formulated nanoparticles

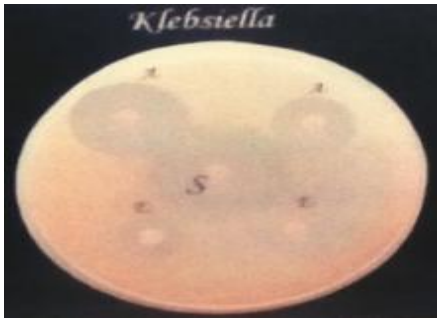
Comparison and release rate of pure drug and formulated nanoparticles

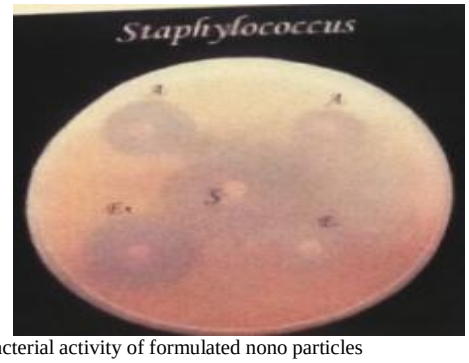
Table – 10

Name of strain	Zone of inhibition in nm				
Bacterial strain	Standard	A1	A2	E1	E2
Klebsiella	19	16	14	11	10
Streptococcus	20	11	15	12	13
Staphylococcus	22	17	12	18	11

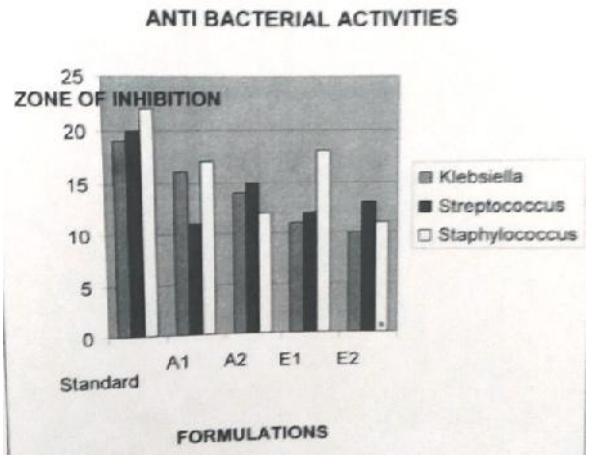
In vitro antibacterial studies was done to confirm the efficacy of the formulation by measuring the zone of inhibition and the result were presented in table X.







Anti bacterial activity of formulated nono particles



SUMMARY AND CONCLUSION:

Cefadroxil an antibacterial drug was loaded in Nano particulate carrier using albumin and polymethacrylate polymers in different ratios by cross linking method and pH-coacervation method. Time, speed of sonication and temperature were standardized to yield good formulation. Drug content and loading analysis confirms the entrapment of drug in the carrier. In vitro release studies of each polymer was evaluated the synthetic polymer was exhibiting more extended release than natural polymer and the proportion have its influence in extending the release rate of the drug. Invitro anti-bacterial studies confirms the efficacy of the antibacterial agent in the formulations, which was done by measuring zone of inhibition. Above studies reveals that the antibacterial activity of cefadroxil can be maintained and extended over a period of time, reducing the frequency of doses.

REFERENCE:

1. Aliautdin, R. N., V. E. Petrov, et al. (1998). "[The delivery of loperamide to the brain by using polybutyl cyanoacrylate nanoparticles]." Eksp Klin Farmakol 61(1): 17-20.
2. Allemann, E., J. C. Leroux, et al. (1993). "In vitro extended-release properties of drug-loaded poly(DL-lactic acid) nanoparticles produced by a salting-out procedure." Pharmacetical Research 10(12): 1732-7.
3. Coester, C. J., K. Langer, et al. (2000). "Gelatin nanoparticles by two step desolvation--a new preparation method, surface modifications and cell uptake." Journal of Microencapsulation 17(2): 187-93.
4. Couvreur, P., E. Fattal, et al. (1991). "Liposomes and nanoparticles in the treatment of intracellular bacterial infections."Pharm Res 8(9): 1079-86.
5. Fontana, G., G. Pitarresi, et al. (1998). "Preparation, characterization and in vitro antimicrobial activity of ampicillin-loaded polyethylcyanoacrylate nanoparticles." Biomaterials 19(11-12): 1009-17.
6. Fresta, M., G. Cavallaro, et al. (1996). "Preparation and characterization of polyethyl-2-cyanoacrylate nanocapsules containing antiepileptic drugs." Biomaterials 17(8): 751-8.
7. Guise, V., J. Y. Drouin, et al. (1990). "Vidarabine-loaded nanoparticles:aphysicochemical study." Pharm Res 7(7): 736- 41.
8. Gulyaev, A. E., S. E. Gelperina, et al. (1999). "Significant transport of doxorubicin into the brain with polysorbate 80-coated nanoparticles." Pharm Res 16(10): 1564-9.
9. Guzman, M., J. Molpeceres, et al. (1993). "Formation and characterization of cyclosporine-loaded nanoparticles." Journal of Pharmaceutical Sciences 82(5): 498-502.
10. Kreuter, J. (1991). "Liposomes and nanoparticles as vehicles for antibiotics." Infection 19(Suppl 4(1)): S224-8.
11. Kreuter, J. (1994). "Drug targeting with nanoparticles." European Journal of Drug Metabolism and Pharmacokinetics 19(3): 253-6.
12. Kreuter, J., R. N. Alyautdin, et al. (1995). "Passage of peptides through the blood-brain barrier with colloidal polymer particles (nanoparticles)." Brain Research 674(1): 171-4.
13. Lin, W., M. C. Garnett, et al. (2001). "Preparation and characterisation of rose Bengal-loaded surface-modified albuminnanoparticles." Journal of Control Release 71(1): 117-26.