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PREPARATION OF MAGNETIC NANOPARTICLES AND CHARACTERIZATION

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ABSTRACT

Levosallbutemol, is a short-acting β_2 adrenergic receptor agonist used in the treatment of asthma and chronic obstructive pulmonary disease. The prepared magnetic nanoparticles of levosalbutamol aims to deliver the drug which passes through oral route as it provides immediate or controlled release of drug when compared to other route of administration. Formulate and characterize the formulation of levosalbutamol to minimize the side effects such as nausea, vomiting, diarrhea. The levosalbutamolmagnetic nanoparticles was successfully prepared by using nanoprecipitation method by taking F02 to F06 formulation by using different concentration of polymer ratio. And as a polymer iron oleate is used and polyvinyl alcohol (PVA) as a stabilizer. The prepared formulations of magnetic nanoparticles was evaluated for various parameters. Levosalbutamolin 1:5 (F06) shows better particle shape and size, SEM study of prepared magnetic nanoparticles were within the range of (1-1000µm). There is no drug excipients interactions in FTIR and DSC. The formulation of F06 showed good particle size with good spherical shape and uniformly distributed without any lumps. The percent drug content was found to be 76.58±0.25% in 10hrs showed anomalous mode of drug release, in F06 formulations.

Keywords: Levosallbutemol, nanotechnology, Nanoparticles, magnetic nanoparticles.

INTRODUCTION

Nanotechnology is the science it means small nano came from the Greek word "Nano" which means dwarf small. Development nanotechnology on the nanometer scale, usually size ranges from 0.1 to 100nm. Nano materials have established many important applications in biomedical, pharmaceutical, electronic, and molecular diagnostic fields. The polymeric nanoparticle (PNPs) is prepared from biocompatible and biodegradable polymers in size between 10-1000nm.Where the drug is dissolved, entrapped, encapsulated (or) attached to a nanoparticle's matrix[1].

Application of nanotechnology: Nano suspensions

They are dispersion of colloidal Nano sized drug particles these are produced by many suitable methods and stabilizer.

Nano emulsion: Nano emulsion is defined as oil/Water emulsions, it consists of mean droplet diameters ranging from 50-1000nm. Usually, the average droplets size in between 100 -500nm.

Nano particles: Nano particles are defined as solid, sub-micron-sized drug carriers that may(or) may not be biodegradable[2]. The term Nano particle is a collective term for both Nano spheres and Nano capsules.

Nano spheres: They have a matrix type of structure. Drug may be absorbed at the sphere surface (or) Encapsulated within the particles.

Magnetic nanoparticles[1-3]

Theseare a class of nanoparticle that can be manipulated using magnetic fields. Such particles commonly consist of two components, a magnetic material, often iron, nickel and cobalt, and a chemical component that has functionality. While nanoparticles are smaller than 1 micrometer in diameter (typically 1–100 nanometers), the larger microbeads are 0.5–500 micrometer in diameter. Magnetic nanoparticle clusters that are composed of a number of individual magnetic nanoparticles are known as magnetic nanobeads with a diameter of 50–200 nanometers. Magnetic nanoparticle clusters are a basis for their further magnetic assembly into magnetic nanochains. The magnetic nanoparticles have been the focus of much research recently because they possess attractive properties which could see potential use in catalysis including nanomaterial- based catalysts, biomedicine and tissue specific targeting, magnetically tunable colloidal photonic crystals, microfluidics, magnetic resonance imaging, magnetic particle imaging, data storage, environmental remediation, nanofluids, optical filters, defect sensor, magnetic cooling and cation sensors.

Physical Principle

Magnetic targeting is based on the principle that the attraction of magnetic nanoparticles to an external magnetic field source gives them the power of targeted drug delivery. When there is a magnetic field, there is a control center manipulating the particle or drug complex. As a result, the drug is delivered effectively to the target location.

The Properties of magnetic nanoparticles

Magnetic nanoparticles be assembled in specific sizes, shapes, and in reasonable quantities. Magnetic nanoparticles can be built to function in various ways. They can be manufactured as monodisperse particles with exactly defined biochemical, electrical, optical, and magnetic properties. They can be tailored to suit the complexity of whatever application they are deliberated for; such gives rise the release of the contents in response to a bi molecular triggering mechanism in targeted drug-delivery system.

1.4 CHARACTERIZATION (OR) EVALUATION OF MAGNETIC NANOPARTICLE[15]

1. DETERMINATION OF THE PH OF MAGNETIC NANOPARTICLES: Magnetic nanoparticles formulation pH was estimated utilizing an advanced computerized pH meter at room temperature. Magnetic nanoparticles scattering pH values drop inside a scope of 3.0-7.5.
2. MEAN MAGNETIC NANOPARTICLES: The mean molecular size of magnetic nanoparticles prepared from performed polymers are in general between 250-500nm. In double emulsification method has concluded that particle size depends on the internal and external surfactants that determine droplet size, the interaction at the interface and the structural conformation of the magnetic nanoparticles wall.
3. DETERMINATION OF DRUG CONTENT: Drug content was controlled by dissolving 1ml of arranged Magnetic nanoparticles in 20ml of acetonitrile. Appropriate amount of sample was then exposed to the UV Spectrophotometer at 232nm. The absorbance for each sample was estimated and contrasted with the standard.
4. PARTICLE SIZE DISTRIBUTATION AND PARTICLE CHARGE/ZETA POTENTIAL: Particle size appropriation is an important aspect during the formulations of nano systems. Magnetic nanoparticles were characterized for their molecule size dissemination and zeta potential using Malvern zeta sizer.
5. STRUCTURAL CHARACTERISATION: Structural characterization should be possible by using field emission scanning electron microscopy (FE-SEM) and transmission electron microscopy (TEM) to determine the various attributes like shape, size, and surface morphology, micrographs of the Magnetic nanoparticles were obtained. Utilizing a Phillips Cm 200 worked at 20-200 Kev while the Fe-SEM was done utilizing Hitachi S-4800 FE-SEM outfitted with Energy Dispersion Spectrometer (EDS).
6. IN-VITRO DRUG RELESE: In vitro drug discharge studies were done utilizing USP type 11 dissolution apparatus. The study was carried out in 100 ml of buffer (PH 3.0). the Magnetic nanoparticles suspension was putdown in dialysis membrane and immersed in dissolution medium which was kept inert thermostatically at 37±0.50C. The stirring rate was maintained at 100 rpm. At predetermined time intervals 5ml of sample were withdrawn and assessed for drug release Spectro photo metrically. After each withdrawal 5 ml of fresh dissolution medium was added to dissolution jar.

MATERIALS AND METHOD

LIST OF MATERIALS

S. NO.	NAME OF THE PRODUCT	NAME OF THE SUPPLIER
1.	Levosalbutamol	MSN Organics Pvt Ltd. Bibinagar, Telangana, India.
2.	Ethanol	TCI Chemical (India)Pvt. Ltd
3.	Iron oxide	Ankit Polymers Industries, Ahmedabad
4.	Oleic acid	Famous chemical Industries, Hyderabad.

5.	Hexane	Taj Pharmaceuticals Ltd. Hyderabad
6.	Water	Geethanjali college of Pharmacy.

Methodology Method Of Preparation

NANOPRECIPITATION METHOD OR INTERFACIAL DEPOSITION OF POLYMERS.

Materials And Formulation

Compositions of LNC-Levosalbutamol and LNC-blank yielding a final volume of 10 ml nanosuspension.

Table 1: Formulations of Levosalbutamol Magnetic nanoparticles

Materials	LNC-Blank (F 01)	1:1	1:2	1:3	1:4	1:5
Levosalbutamol	_	25mg	25mg	25mg	25mg	25mg
Ethanol	25 ml	25ml	50ml	75ml	100ml	125ml
Iron oxide	40 mg	40mg	40 mg	40 mg	40 mg	40 mg
Oleic acid	0.4 ml	0.4 ml	0.4 ml	0.4 ml	0.4 ml	0.4 ml
Hexane	50 ml	50 ml	50 ml	50 ml	50 ml	50 ml
Water	50 ml	50 ml	50 ml	50 ml	50 ml	50 ml

Preparation of nanoparticles

Levosalbutamol – loaded magnetic nanoparticles were prepared by coprecipitation method. This method is also known as interfacial deposition of polymer. In this method magnetic nanoparticles creating a colloidal suspension between two separate phases such as organic and aqueous phase. Organic phase consists of drug i.e.Levosalbutamol(25mg) and base ethanol (25 ml,50 ml,75 ml,10ml,125 ml) in different ratios (1:1,1:2,1:3,1:4,1:5). polymer solubilized in oleic acid (oil-0.4 ml) previously. Aqueous phase consists of Fe2+ and Fe3+ with water (50 ml). Then organic phase injected slowly as dropwise into aqueous phase under constant speed of magnetic stirring for 10 min. Closing volume was adjusted in a volumetric flask up to 10 ml. Blank nanoparticles were prepared similarly but without addition of Levosalbutamol to oleic acid .The size, shape, and composition of iron NPs synthesized through chemical methods depend on the type of salt used, Fe2+ and Fe3+ ratio, pH, and ionic strength.

EVALUATIONS OF MAGNETIC NANOPARTICLES

a) Scanning electron microscopy (SEM)

Scanning electron microscopy was used to determine surface topography, particle size, texture and by the SEM we can detect the size and morphology of broken or sectional surface. So, the dried levosalbutamol nanoparticles were kept on the electron microscope stub which was covered with a black adhesive tape. Later, these Nanoparticles were coated with gold and examined under vaccum at room temperature. The Nanoparticles were observed at accelerated voltage of 1000 volts.

b) Differential scanning calorimetry (DSC)

DSC is carried out by the physical state of Levo salbutamol on nanoparticles were analyzed by differential scanning colorimeter. Thermogram of pure drug, pure polymer and drug loaded nanoparticles were obtained at a scanning rate of over a temperature vary of 250.28˚C. DSC determines that the temperature range and heat rate. And by this DSC we can find quantitative and qualitative information on endothermic (heat absorption) exothermic (heat evolution process of materials) during physical transition.

c) Drug and polymer interaction study (FTIR)

FTIR spectroscopy was performed on the Fourier transform infrared spectrophotometer and it is used to study and find out whether there is any physical and chemical interactions between the drug and polymer used in the formulation. And, to know the stability of the drug during coprecipitation process.

d) In vitro dissolution drug release study

By using dissolution apparatus which is carried out in USP dissolution apparatus-II. 900ml of dissolution medium (distilled H2O) was placed into each vessel and the apparatus was assembled. Then the medium was allowed to equilibrate to a temperature of 37±0.5℃. 100mg of all formulations was placed into each vessels and operated at 50rpm. After 1hr, 5ml of dissolution medium is withdrawn and replaced with 5ml of dissolution medium into the same vessel. The same process was repeated for 4hrs, four concentration were collected for each 1hr. And then it was filtered and transferred into UV spectrophotometer were noted at 272nm.

4. RESULTS& DISCUSSIONS

INCOMPATIBILITY STUDIES

1. Drug excipients interaction study: FTIR

This is carried out using FTIR which is used to analysis the physicochemical interactions between the active substance and excipient used in the dosage form. Drug excipients' interactions play an important function in the discharge of the drug from the formulation. The pure Levosalbutamol and its blended with each of different concentrations of iron oleate were scanned by using FTIR instrument. The drug exhibits

peak due to ketonic group, broad peak of alcohol group and C=C stretching which is shown in Figure 4.2. It was noticed that there were no changes in these main peaks in the IR spectra of a mixture of drug and polymers [Figures 4.3]. The FTIR study revealed no physical or chemical interactions of Levosalbutamol with iron oleate as evident.

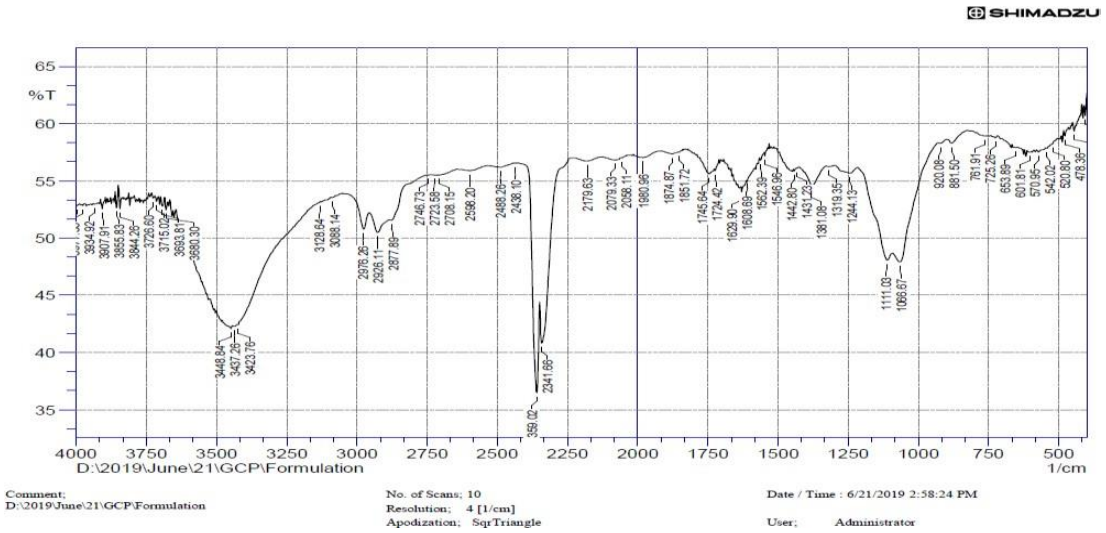

Fig 1: FTIR of Pure Levosalbutamol

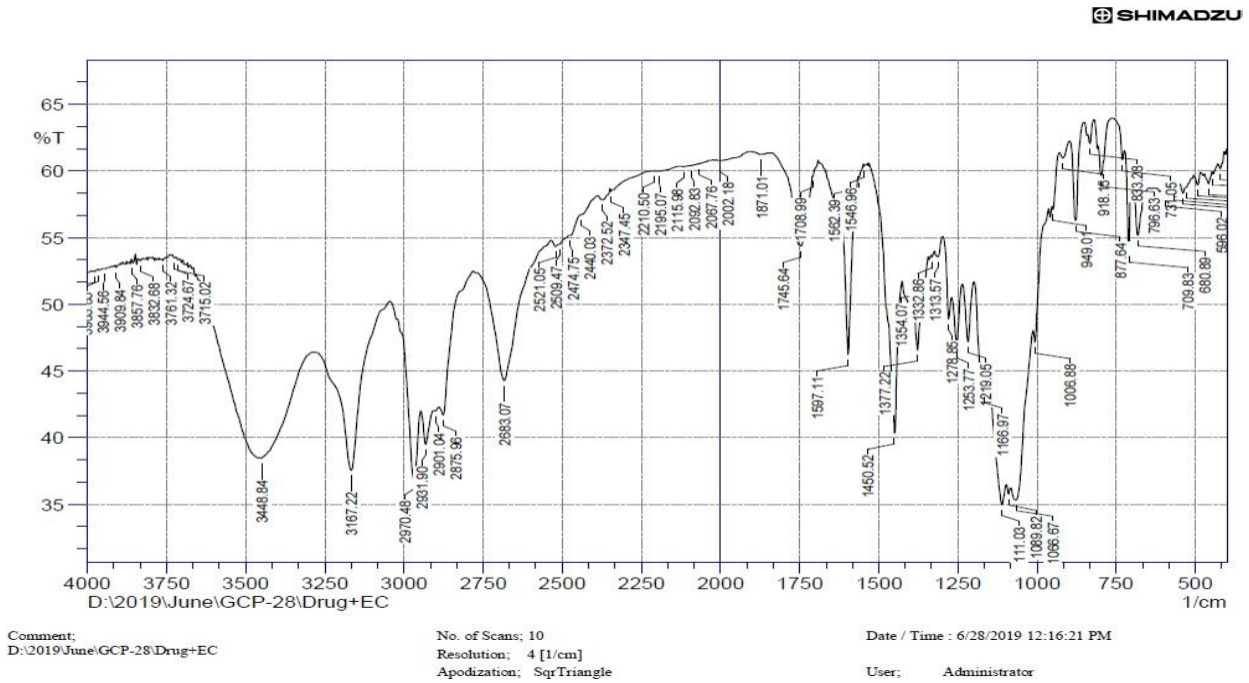

Fig 2: FTIR of Levosalbutamol and Excipients (iron oleate)

2.Differential Scanning Calorimeter (DSC)

DSC is an effective thermal analyzer which measures the property of variety of materials ranging from150 to600°C. It offers quantitative and qualitative details about endothermic (heat absorption) and exothermic (heat evolution) system of material.

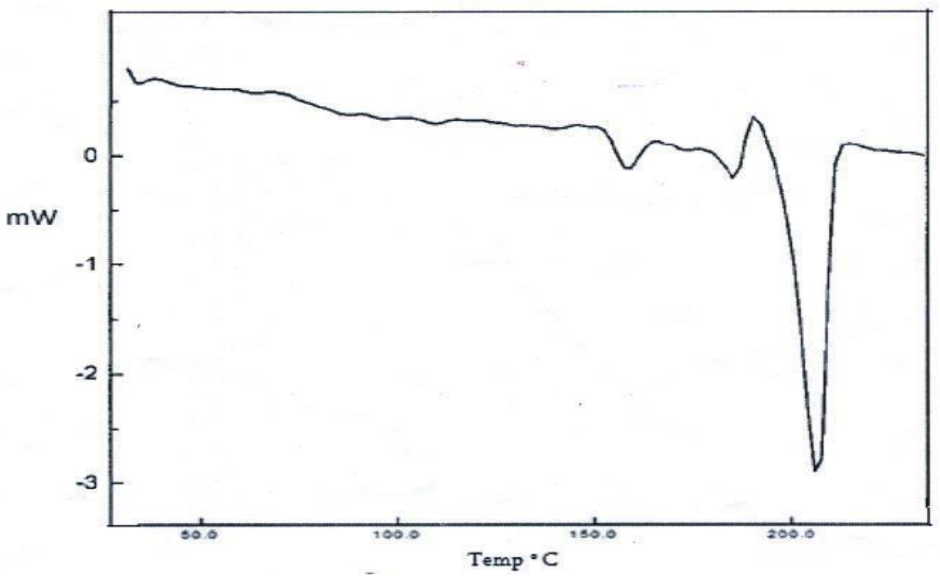

Fig 3: DSC of Pure Levosalbutamol.

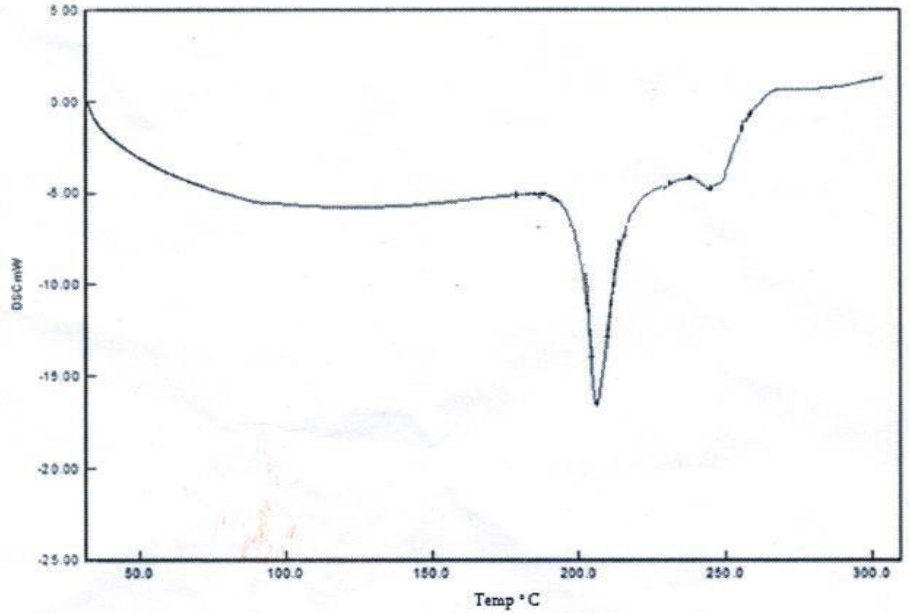

Fig 4: DSC Of Levosalbutamol Magnetic nanoparticles

3. Scanning Electron Microscope

SEM revealed that the shapes of magnetic nanoparticles.

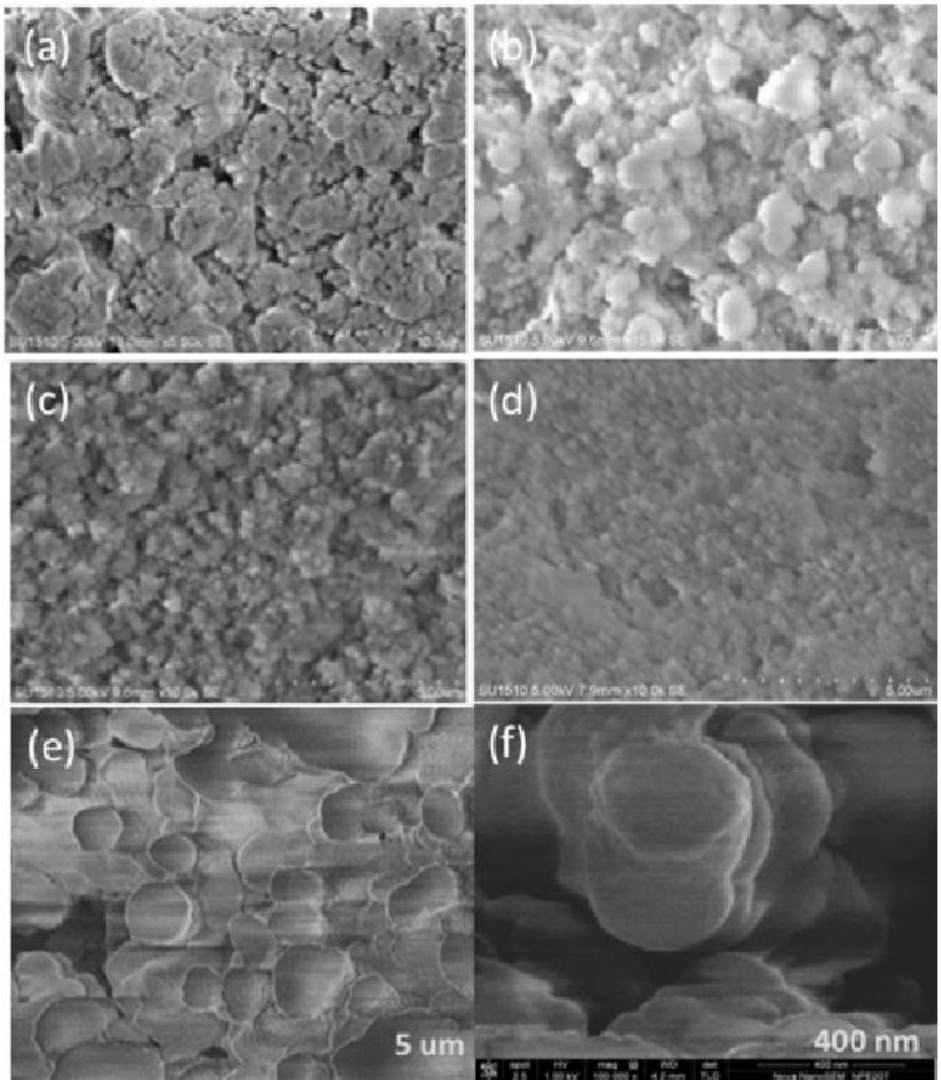

Fig 5: SEM of Nanoparticles

4.In vitro drug release studies

The dissolution research had been carried out in USP type II apparatus using 0.1N HCl as a medium, maintained at a temperature of 37^0C for about 10 hours. • Drug release was calculated utilizing the next formulas

$$\% \text{ drug release} = \frac{\text{amount of sample (mg)}}{\text{dose (mg)}} \text{ x } 100$$

$$\% \text{ cumulative drug release} = \frac{\text{volume of sample withdrawn (ml)}}{\text{bath volume (ml)}} \text{ x } P(t-1) \text{x } Pt$$

Where

P (t-1) = percent drug release before time 't'
Pt = percent drug release at time 't'

Table 2:Cumulative percent drug release profile

Time	Formulation	Formulation	Formulation	Formulation	Formulation	Formulation
1hr	10.26±0.12	11.79±0.38	12.6±0.54	14.4±0.65	15.21±0.72	**16.83±0.28**
2hr	14.46±0.91	15.26±0.68	16.88±0.22	18.85±0.63	19.42±0.54	**20.44±0.75**
3hr	21.13±0.51	23.75±0.42	24.64±0.75	25.35±0.85	26.40±0.49	**27.82±0.61**
4hr	29.55±0.54	31.16±0.61	32.88±0.84	34.61±0.31	35.41±0.61	**37.11±0.24**
5hr	36.25±0.43	37.56±0.12	38.76±0.35	42.09±0.62	43.83±0.75	**48.87±0.20**
6hr	40.50±0.24	45.46±0.32	46.35±0.43	48.00±0.62	51.57±0.86	**56.40±0.53**
7hr	44.65±0.21	49.72±0.12	51.35±0.19	56.69±0.53	58.10±0.62	**64.00±0.39**
8hr	58.12±0.01	60.65±0.22	63.19±0.29	64.53±0.18	66.58±0.90	**70.70±0.74**
10hr	64.82±0.71	65.61±0.56	69.04±0.46	73.52±0.82	75.44±0.19	**76.58±0.25**
12hr	68.17±0.73	69.62±0.92	73.22±0.72	76.59±0.64	79.12±0.53	**80.84±0.09**

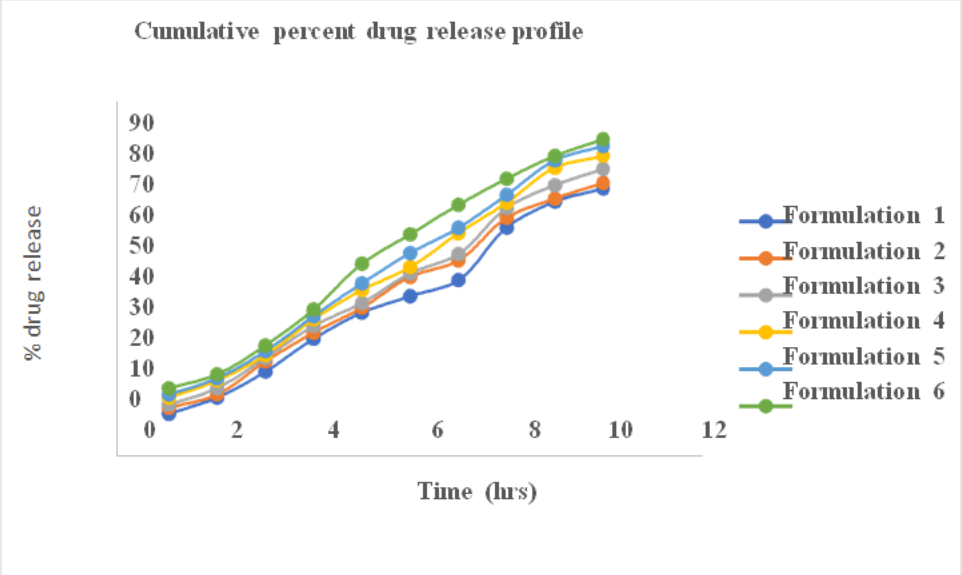

Fig 6: Cumulative percent drug release profile

Invitro drug release study for all the six formulations were carried out for12hrs and tabulated shown in table 4.2. The results obtained proved that the invitro release influenced by polymer ratios. The Magnetic nanoparticles containing iron oleate at different ratios has shown drug release at various percentages as shown in above table 4.2. These variations in drug release were due to changes in polymer concentration on magnetic nanoparticles. Formulations F 06 met the desired drug release profile in 12hr.Therefore, thought of one of the best formulation around all the formulations

CONCLUSION

Levosallbutemol, is a short-acting β_2 adrenergic receptor agonist used in the treatment of asthma and chronic obstructive pulmonary disease. The prepared magnetic nanoparticles of levosalbutamol aims to deliver the drug which passes through oral route as it provides immediate or controlled release of drug when compared to other route of administration. Formulate and characterize the formulation of levosalbutamol to minimize the side effects such as nausea, vomiting, diarrhea. The levosalbutamolmagnetic nanoparticles was successfully prepared by using nanoprecipitation method by taking F02 to F06 formulation by using different concentration of polymer ratio. And as a polymer iron oleate is used and polyvinyl alcohol (PVA) as a stabilizer. The prepared formulations of magnetic nanoparticleswas evaluated for various parameters. Levosalbutamolin 1:5 (F06) shows better particle shape and size, SEM study of prepared magnetic nanoparticles were within the range of (1-1000µm). There is no drug excipients interactions in FTIR and DSC. The formulation of F06 showed good particle size with good spherical shape anduniformly distributed without any lumps. The percent drug content was found to be 76.58±0.25% in 10hrs showed anomalous mode of drug release, in F06 formulations.

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