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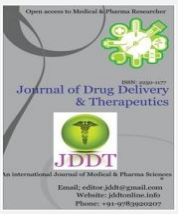

Open Access Research Article

FORMULATION AND EVALUATION OF IVERMECTIN SOLID DISPERSION

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ABSTRACT

This study was aimed to formulate and evaluate solid dispersion containing ivermectin to improve solubility. Ivermectin is BCS (Biopharmaceutical classification system) class-II drug, which has high permeability and low water solubility (0.005mg/ml) which is responsible for its poor dissolution rate and ultimately leads to variable absorption. Solid dispersion with Gelucire (44/14) has the ability to improve dissolution of poor water soluble drugs. So, solid dispersion ivermectin with Gelucire 44/14 was prepared to enhance the solubility and was further evaluated for different parameters such as assay, wettability, DSC, FT-IR, dissolution study.

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INTRODUCTION:

Helminthiasis is the type of intestinal tract infection. Sometimes they may involve with other organs. The human body is with a parasitic worm such as roundworms and pinworms. The worms are usually present only in the intestinal tract. The severity of symptoms is classified by the type of worm and the part of the body infected. Ivermectin is the medication that is effective against many types of parasites. It is used to treat- Helminthiasis, Head lice; Scabies, Lymphatic filariasis, River blindness and Strongyloidiasis. Ivermectins are macro cyclic lactones derivatives[1]. It is derived from the bacterium Streptomycin avermitilis. Ivermectin kills by interfering with nervous system and muscle function, in particular by enhancing inhibitory neurotransmission. 3.0 mg and 6.0 mg tablets of ivermectin are available as marketed preparations[2]. Solid dispersion is defined as one or more active ingredients in an inert carrier or matrix at solid state prepared by the fusion-solvent or melting-solvent method. A product formed by converting a fluid drug-carrier combination to the solid state[3]. Solid dispersion defines the texture of two different parts. One is the water soluble carrier and another is water in-soluble (polar) compounds. A carrier it can be either crystalline or amorphous in nature. They are based according to their drug molecular structure[4].

MATERIALS AND METHODS:

Materials

Ivermectin, Gelucire 44/14, Distilled Water, Aspartame, Methanol, Hydrochloric acid, Lactose, HPMC (hydroxypropyl methylcellulose), SSG (sodium starch glycolate), MCC (microcrystalline cellulose), Magnesium Stearate, Talc.

Methods

For preparation of solid dispersion: Different methods involves physical mixture, melting, kneading

method, lyophilization, solvent evaporation, melt agglomeration process, extruding method, spray drying technology, use of surfactant, electro static spinning method and super critical fluid technology[5].

Physical Mixing

Physical mixing method of Gelucire 44/14 with drug is prepared by geometric mixing of drug & carrier respectively without applying pressure. An excess quantity of drug & carrier is taken in a glass mortar and mix for 20 minutes.

Melting Method

In Melting method the carrier Gelucire 44/14 is dissolved at 40^0c. After the melting process, add drug. They are proper miscible of mixture. Immediately the mixture is cooled in freezing point. or at room temperature. After cooling the samples they were scrapped out. And dried powder is passes through sieve no 100#.

Kneading Method

Solid dispersion by Kneading method is prepared by symmetrical mixing of drug with Gelucire 44/14. After mixing they were kneaded with appropriate ratio of solvent's fusion to get and extent with a pasty consistency, which is dried in hot air oven at 45˚ to 50˚C. The dried powder is passes through sieve no 100#.

Lyophilization Technique

In lyophilization process, the matrix & drug are dissolved in suitable solvent. After the geometric mixing of solution they are cooled& freeze dried in Vir-Tis Benchtop K lyophilizer (freeze drier) to 24 hrs. After lyophilization, get % yield amorphous powder. The dried solid dispersions were sieved through 100#.

Characterization of solid dispersion

Prepared solid dispersion can be characterized by differential scanning calorimetry (DSC) analysis, infrared (IR) analysis, wettability study, in-vitro dissolution study and effect of different formulation variables on various evaluation parameters[6].

Formulation of tablets using solid dispersion

Tablets were formulated using solid dispersion containing equivalent quantity of 3 mg of Ivermectin by different techniques like (I) Physical mixing, (II) Melting method, (III) Kneading method, and (IV) Lyophilization. Plain tablet of Ivermectin (3mg) without Gelucire 44/14 was also prepared for comparison in the dissolution behaviour. All these tablet formulations were prepared using direct compression techniques with necessary excipients shown in table 1.

Table 1: Excipients used in tablets containing plain Ivermectin, and with solid dispersion

Excipients	Plain Ivermectin Tablet (mg)	Tablet with Ivermectin & solid dispersion(mg)
Drug	3	33
SSG	10	10
MCC	20	20
Magnesium stearate	2	2
Talc	2	2
Aspartame	5	5
Menthol	2	2
Lactose	Uptoq.s.	Uptoq.s.
Total	300	300

Characterization of tablets

All these tablet formulations should be evaluated by various parameters such as size, shape, weight variation, hardness, friability, thickness, drug content, disintegration and in-vitro dissolution study.

RESULT AND DISCUSSION:

Table 2: Evaluation parameters of MDT tablet prepared using solid dispersion by melting method

Parameter	Value
Size-Diameter	7.2 mm
Shape	Round
Color	White
Thickness	4 mm
Hardness	4.5 Kg/cm^2
Weight variation	275.6 mg
Drug content	96.25 %
Disintegration time	3-4 min

In-vitro dissolution study of tablet formulation

In-vitro dissolution study of tablet formulation was carried out in 0.1 N HCland presented in Figure 1.

From this dissolution studies, it can be seen that the tablets prepared using solid dispersion by melting method showed highest cumulative % drug release (100% in both 0.1 N HCL)in comparison of plain Ivermectin. The tablets prepared using solid dispersion by other methods like physical mixing, kneading method, and lyophilization also showed in improvement of drug release in comparison to tablets prepared with plain Ivermectin. All these tablet formulations showed the maximum drug release in 90 minutes. Hence, melting method formulation was found the best formulation which gave highest % drug release at the end of 105mins.

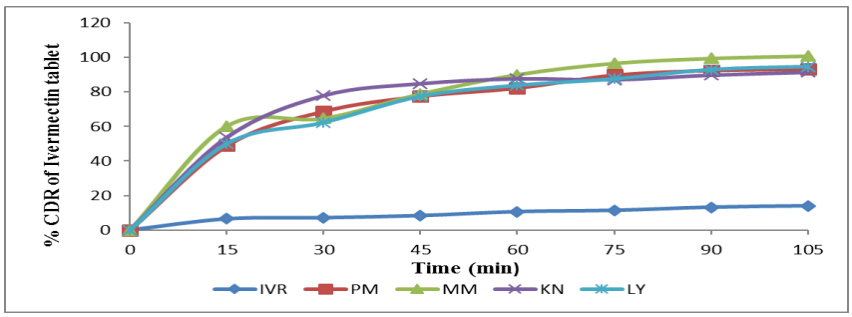

Figure 1: Dissolution profile MDT tablet of plain Ivermectin and PM, MM, KN & LY in 0.1 N HCL.

Table 3: % CDR of Tablet formulations in 0.1 N HCL in dissolution

Time (min)	% CDR of Tablet formulations				
	Ivermectin	**PM**	**MM**	**KN**	**LY**
15	6.45	48.92	60.22	53.76	50.00
30	7.12	68.72	64.65	77.26	62.29
45	8.33	77.60	78.82	84.87	77.49
60	10.65	82.33	90.02	87.69	83.89
75	11.39	89.82	96.58	87.11	87.59
90	13.22	92.58	99.47	89.81	93.00
105	14.00	93.22	100.77	91.45	94.72

CONCLUSION:

After optimizing the ratio of drug and carrier (1:10 %w/w) by phase solubility studies, Ivermectin solid dispersion was successfully prepared by different methods like physical mixture. These solid dispersions confirm the entrapment of Ivermectin in the Gelucire 44/14 by DSC and FTIR studies. All prepared solid dispersion of Ivermectin showed improvement in the Wettability and dissolution profile of Ivermectin. Highest improvement in the in-vitro dissolution profile was obtained in the solid dispersion prepared by melting method. Tablet formulation prepared using solid dispersions by melting method showed highest improvement in the dissolution profile in comparison to other solid dispersions as well as plain Ivermectin. Finally it can be concluded that poor dissolution profile of water insoluble Ivermectin can be overcome by preparing its solid dispersion with Gelucire 44/14.

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