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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET OF ALBENDAZOLE BY USING A CO-CRYSTAL TECHNIQUE

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ABSTRACT

Background: Albendazole is used as an anthelminthic. It is a BCS class II drug having poor aqueous solubility. **Objective:** This study was aimed to formulate and evaluate fast-dissolving tablets of containing co-crystals of Albendazole for the improvisation of critical attributes of the product such as dissolution rates, solubility and oral bioavailability. **Methods:** Co-crystals were prepared by Solvent Evaporation method using Natural gums such as Xanthan gum as co-formers. Tablets were compressed by using direct compression method using SSG and Crospovidone as super disintegrants in different concentration. **Results:** Pre-formulation studies were performed and evaluation of prepared co-crystals revealed that Co-crystals formulated with Xanthan gum showed best results. The manufactured fast-dissolving tablets were evaluated for different parameters including weight variation, hardness, thickness, friability, drug content, In-vitro disintegration and In-vitro dissolution studies. Formulation F4 shows significant change in dissolution rate and also helped to increase the solubility of poorly water- soluble drugs and both of them i.e. solubility and percentage of drug release are the key factors to exhibit the efficiency of the drug. Formulation of co-crystal with Xanthan gum in 1:1 ratio showed highest drug content (99%) using Crospovidone. **Conclusion:** According to the result obtained, fast-dissolving tablet containing co-crystals of albendazole enhances the dissolution rate, solubility and hence increases the therapeutic efficacy and could be considered convenient oral delivery systems to enhance the drug bioavailability.

KEYWORDS: Albendazole, co-crystal, co-former.

INTRODUCTION

DEFINITION OF CO-CRYSTAL: Co-crystals are multicomponent molecular crystals where all components are at a stoichiometric ratio and comprise of two or more chemically different molecules includes modification of drugs to alter physical properties of a drug, especially a drug's solubility without altering its pharmacology effect.

The main advantage of the technique is that it can improve physical properties such as solubility, dissolution, and compressibility, without affecting the pharmacological activity of the API. This is due to the presence of co-formers in the crystal structure which is a component of modifying physical properties.

A cocrystal is composed of two components. The first component is the API, and the second component is called a co-former.

DEFINITION OF CO-FORMERS: A component that interacts non-ionically with the API in the crystal lattice, that is not a solvent(including water),and is non-volatile.
In general, the ratio between API and co-former is 1:1,1:2, or vice-versa cocrystal with API that acts as a co-former are called co-crystal drugs.

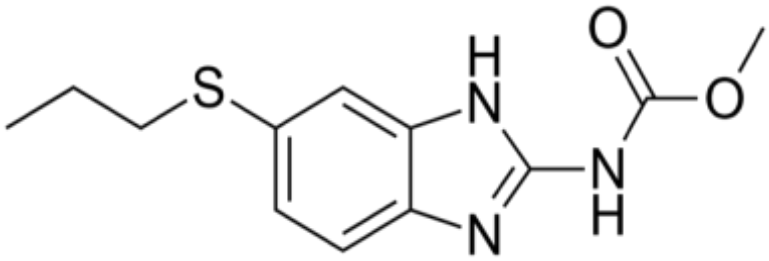
DIFFERENT METHODS USED FOR COCRYSTALS FORMATION

1. Solvent Evaporation Method
2. Grinding Method
3. Hot Melt Extrusion
4. Microwave Assisted Synthesis
5. Spray drying technique
6. Ultrasound Assisted Solution Co-crystallization

CHARACTERIZATION OF CO-CRYSTALS

Physical: Solubility, Melting point.

DRUG PROFILE



1. CHEMISTRY

Chemical name : Albendazole

Synonyms : Albenza, Andazol, Eskazole, Zentel

IUPAC Name : methyl-[5-(propylthio)-1H-benzoimidazol-2-yl] carbamate

Molecular formula : C12H15N3O2S

Molecular weight : 265. 333 g/mol

2. DESCRIPTION

Colour : White to off-white powder

Melting point : 208 c to 210 c

Percentage purity : > or equal to 98%

Solubility : Soluble in Dimethyl sulfoxide, Strong acids & bases
Slightly soluble in methanol, chloroform, acetonitrile
Practically insoluble in water

Class : A synthetic Anti-helminthic belongs to class Benzimidazoles

3. SPECTRAL INFORMATIONS

UV Spectra: Maximum Absorbance at 300nm

5. MECHANISM OF ACTION

Albendazole sulfoxide, an active metabolite of Albendazole causes selective degeneration of cytoplasmic microtubules in intestinal and tegumental cells of intestinal helminths and larvae by diminishing its energy production, ultimately leading to immobilization and death of the parasite.

7. DOSAGE FORM:- Tablet(oral)

8. INDICATION AND CLINICAL USE:- Medication for treating a variety of parasitic worm infections such as, for the treatment of parenchymal neurocysticercosis due to active lesions of the nervous system caused by larval forms of the pork tapeworm, *Taenia solium* and for the treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus*.

EXPERIMENTAL WORK

I) PREPARATION OF ALBENDAZOLE CO-CRYSTALS:

SOLVENT EVAPORATION METHOD

ALB Co-crystals were prepared by a solvent evaporation method using Xanthan gum in different ratios (1:1 of the drug: polymer). A minimal amount of methanol was used to dissolve the required amount of ALB and the carrier by continuous stirring with a magnetic stirrer for one hour at room temperature. The solvent was completely removed under reduced pressure using a rotary evaporator kept at 40 °C. The Co-crystals formed were further dried in an oven at 40° for 24 hours. All the resulting solid materials were scraped, pulverized in a mortar and sieved through a 60-mesh sieve. Following that, all co-crystals were stored in amber glass bottles and kept in the desiccator until further use.

II) PREFORMULATION STUDIES

1) Angle of Repose
2) Bulk Density
3) Tapped Density
4) Carr’s Compressibility Index
5) Hausner Ratio

FORMULATION DESIGN

Preparation of Albendazole Fast Dissolving Tablets

All additional excipients and a precisely weighed quantity of Albendazole co-crystals were filtered through a 60-mesh sieve before being combined in a mortar and pestle for 30 minutes. A single punch tablet machine was used to immediately compress the mixture into tablets. With the exception of the super disintegrant and the binder, all excipient quantities remained constant as given in table.

S.No.	Ingredients	F1(mg)	F2(mg)	F3(mg)	F4(mg)
1.	Albendazole Co-crystals	400	400	400	400
2.	SSG	10	20	-	-
3.	CP	-	-	10	20
4.	MCC	50	40	50	40
5.	Mannitol	25	25	25	25
6.	Aspartame	5	5	5	5
7.	Magnesium stearate	5	5	5	5
8.	Talc	5	5	5	5

V) EVALUATION OF ALBENDAZOLE FAST DISSOLVING TABLETS

1) Weight Variation Test
2) Thickness Test
3) Hardness Test
4) Friability Test
5) Wetting time Test
6) In Vitro Drug Release Study

RESULTS AND DISCUSSION

I) PREPARATION OF STANDARD CALIBRATION CURVE

a) Determination of λmax

Preparation of 0.1N Hydrochloric acid

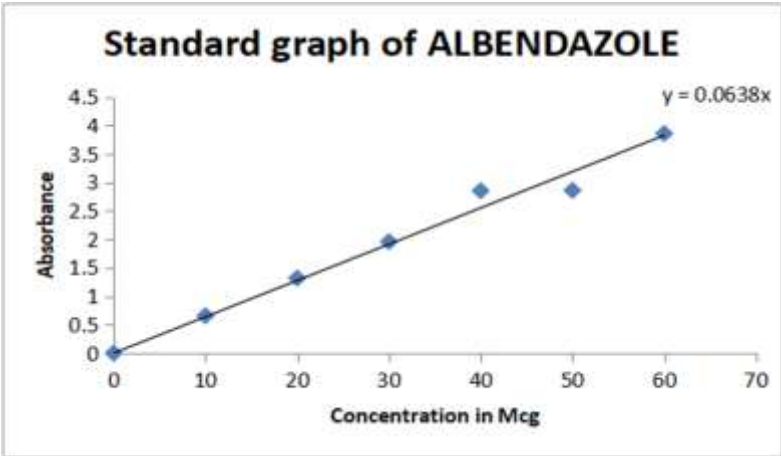
A known volume of 8.5ml Hydrochloric acid is dissolved in distilled water and the volume is made up to 1 litre.

The absorption maximum(λmax) of the Albendazole was estimated by scanning the drug solution(10µL/ml) between 200-400nm regions on UV spectrophotometer.

The λ max was found to be 300 nm in chloroform.

Calibration curve of Albendazole in Chloroform

CONCENTRATION (mcg/ml)	ABSORBANCE
0	0
10	0.657
20	1.318
30	1.959
40	2.853
50	2.86
60	3.86



II) EVALUATION OF CO-CRYSTALS

a) Melting point and solubility

Co-crystal melting values were lower than those of Albendazole. Melting point depression revealed multi-component systems and indicated co-crystal formation. This contact causes a modification in the molecular arrangement, resulting in a new crystal structure with altered solubility(increased) and/or melting point.

Drug/co-former	Melting point
Albendazole	208 C -210 C
Albendazole-Xanthan gum	200 C

III) PRE-COMPRESSION PARAMETERS

Parameter	F1	F2	F3	F4
Bulk density(gm/cm3)	0.35	0.31	0.39	0.33
Tapped density(gm/cm3)	0.55	0.52	0.53	0.59
Hausner ratio	1.4	1.31	1.41	1.39
Compressibility index(%)	27.36	27.28	27.50	27.25
Angle of Repose	37.64	37.5	37.71	36.96

IV) POST-COMPRESSION PARAMETERS

The resulted data of post compression parameters revealed that all the prepared tablets had uniform weight. Weight variation and thickness were found to be in acceptable range. Tablet hardness was retained in range of 4.96-5.38 kg/cm2 for all the tablets. Friability was also in acceptable range between 0.41 to 60%.

Table: Post compression parameters result.

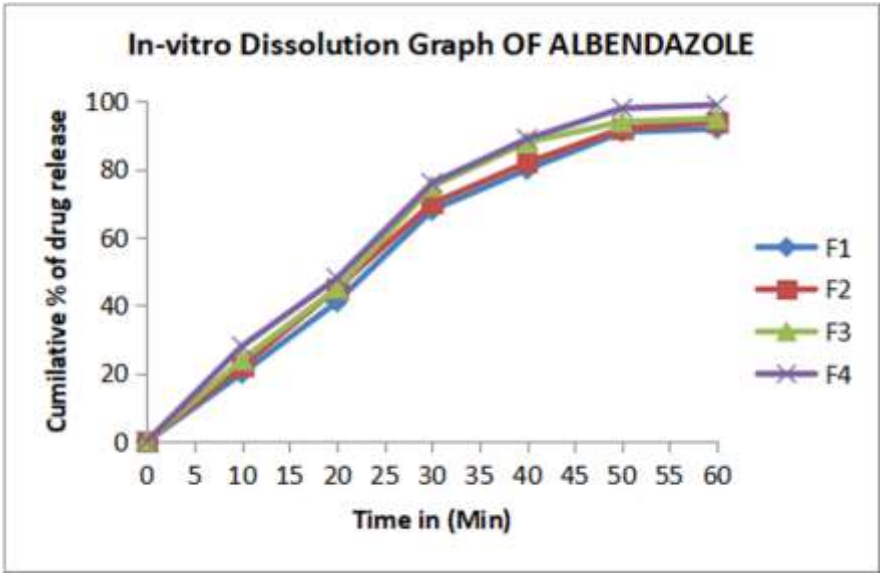
Formulation	Weight variation (mg) ± SD	Hardness (kg/cm2)	Thickness (mm)	Friability (%)	Wetting time
F1	496 ± 4.89	4.96 ± 0.08	1.04 ± 0.05	0.41	24.4 ± 0.48
F2	498 ± 4.0	5.22 ± 0.16	1.06 ± 0.05	0.50	24.6 ± 0.48
F3	494 ± 4.89	5.34 ± 0.37	1.06 ± 0.05	0.59	24.2 ± 0.74
F4	494 ± 4.89	5.38 ± 0.30	1.06 ± 0.05	0.60	24 ± 0.63

n=5

A) IN-VITRO DRUG RELEASE

In-vitro studies showed that formulation with Crospovidone, obtained higher drug release. Formulation F4 showed highest drug release (99%) while formulation F3 had lowest drug release (95%). The results obtained are given below in Table.

Time (Min)	F1	F2	F3	F4
0	0	0	0	0
10	20 ± 0.632	21.2 ± 0.74	23 ± 0.8	27.2 ± 0.7
20	41 ± 0.632	44.6 ± 0.8	46 ± 0.8	47.8 ± 0.7
30	68 ± 0.748	69.6 ± 0.48	75 ± 0.7	76 ± 0.7
40	80.2 ± 0.748	80.8 ± 0.9	87 ± 0.8	88.9 ± 0.6
50	90.9 ± 0.8	91.8 ± 0.7	94 ± 0.6	98 ± 0.8
60	91.2 ± 0.748	92 ± 1.4	95 ± 0.6	98.9 ± 0.6



CONCLUSION

Fast dissolving tablets of ALBENDAZOLE were pre pared by co-crystallization technique and were evaluated for physical parameters like Content of Uniformity, Thickness, Hardness, Friability, Wetting Time, Disintegration. The obtained values are meet the specified monograph. In Vitro dissolution test was performed for the prepared formulations F1 to F4 among F4 was able to release the medicament up to 99 % for a period of 60 min which when compared to F1, F2 and F3. Hence it is concluded that F4 is a best formulation.

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