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Preformulation studies for Amoxicillin trihydrate and Dicloxacillin sodium as Mouth Dissolve tablets

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Abstract: Preformulation is the first step in the rational development of dosage form of a drug substance and it is defined as an investigation of physical chemical properties of a drug substance alone and when combined with excipients. Differential scanning calorimetry was used to examine the thermal behaviour of mixtures of the drug Amoxicillin trihydrate and Dicloxacillin sodium with standard excipients (Croscarmellose Sodium, Pregelatinized starch, Microcrystalline cellulose), to investigate inclusion complexation which could increase the photostability of the drug.
Key words: DSC, Excipients, Amoxicillin trihydrate, Dicloxacillin sodium.

Introduction

In recent years, the mouth dissolve tablet has attracted the interest of many researches. Many pediatric and Geratric patients have difficulty in swallowing tablets, capsules or powders. [1] The basic approach used in the development of fast-dissolving tablets is the development of fast-dissolving tablets is the use of superdisintegrants. They act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration. Another approach used in developing such tablets is maximizing pore structure of the tablets. Freeze-drying [2] and Vacuum-drying techniques.[3]

Preformulation commences when a newly synthesized drug shows sufficient pharmacologic promise in animal models to warrant evaluation in man. These studies should focus on those physicochemical properties of the new compound that could affect drug performance and thorough understanding of these properties may ultimately provide a rationale for formulation design. Areas of preformulation were Bulk characterization, Solubility Analysis, Stability Analysis.[4]

During the development of a solid dosage form, assessment of possible incompatibilities between a drug and different excipients is an important part of the preformulation stage prior to large scale development trails. Excipients are required to facilitate administration, to promote consistent release and bioavailability of the drug, and to protect the active ingredients from the environment. Even though excipients are usually regarded as medically inert, physical and chemical interactions with drugs are common place. Techniques for screening drug-excipient mixtures for compatibility include: a) isothermal stress testing and b) thermal analysis using DSC or DTA.

Differential scanning calorimetry (DSC) used to measure the heat loss or gain resulting from physical or chemical changes with in a sample as a function of temperature. Examples of endothermic (heat-absorbing) processes are fusion, boiling, sublimation, vaporization desolvation, solid-solid transitions, and chemical degradation. Crystallization and degradation are usually exothermic processes. Quantitative measurements of these processes have many applications in preformulation studies including purity,[5] polymorphism,[6] salvation[7] degradation, and excipient compatibility[8-9] is by photo satability

ICH Q1B guideline is the harmonized effort to standardize photostability testing on new pharmaceutical drug substances and drug products. [10-14]

The aim of present study was to evaluate the compatibility of anti bacterial drug Amoxicillin trihydrate and Dicloxacillin sodium and excipients such as Croscarmellose Sodium [15], Pregelatinized starch, Microcrystalline cellulose for their photo stability in tablet formulations.

Materials and Methods

DSC-60(Shimadzu type), Amoxicillin trihydrate and Dicloxacillin Sodium as a gift sample from suriyan pharmaceutical pvt Ltd chennai, Excipients as a gift sample from BASF India Ltd Chennai.

Method of analysis:

Amoxicillin and Dicloxacillin were mixed with excipients in different ratio the mixture is kept in 2ml glass vials and exposed to 25°C/45%RH and 40°C/75%RH for one month. The drugs are mixed with the excipients in the ratio 1:02 and 1:10 and are subjected to different temperatures. The study was done for one month and the observations are given in the Table. 1-3, and their chromatogram is shown at Fig 1-4.

Discussion

The Table1 shows the inference of selected excipients with drug (amoxicillin trihydrate). From these results it was concluded the excipients was suitable to formulate the Dispersible tablet of Amoxicillin and Dicloxacillin DSC thermogram is shown at Fig:1

The Table 2 shows the inference of selected excipients with drug (Dicloxacillin sodium). From these results it was concluded the excipients was suitable to formulate the Dispersible tablet of Amoxicillin and Dicloxacillin. DSC thermogram is shown at Fig: 2-4.

The Table 3 shows the interence of selected excipients with drug (amoxicillin trihydrate & Dicloxacillin sodium).

Conclusion

From the above DSC studies it was concluded that the excipients were photo stable and passed preformulation studies. Excipients are suitable to formulate the Dispersible tablets of Amoxicillin trihydrate and Dicloxacillin sodium.

Table No. 1: Preformulation study of Amoxicillin Trihydrate

S.NO	Excipients	D:E Ratio	Initial	25°C/60%RH		40°C/75RH	
				2nd week	4th week	2nd week	4th week
1.	Ethyl cellulose	1:0.5	NC	NC	NC	NC	NC
2.	Hydroxypropyl Mthyl cellulose	1:1	NC	NC	NC	•	•
3.	Croscarmellose Sodium	1:1	NC	NC	NC	NC	NC
4.	Microcrystalline	1:10	NC	NC	NC	NC	NC
5.	Starch	1:2	NC	NC	NC	NC	NC
6.	Pregelatinized starch	1:1	NC	NC	NC	NC	NC
7.	Sunset yellow supra	1:0:2	NC	NC	NC	NC	NC
8.	Sunset yellow lake	1:0:2	NC	NC	•	•	•
9.	Sodium lauryl sulphate	1:0:5	NC	NC	NC	•	•
10.	Aspartame	1:0:2	NC	NC	NC	NC	NC
11.	Saccharin Sodium	1:2	NC	NC	*	*	*
12.	Sucrose	1:5	NC	NC	•	•	•
13.	Golden Caramel	1:0:2	NC	NC	NC	NC	*
14.	Orange dry flavour	1:0:2	NC	NC	NC	NC	NC
15.	Pineapple dry flavour	1:0:2	NC	NC	NC	NC	NC
16.	Colloidal silicon dioxide	1:1	NC	NC	NC	NC	NC
17.	Talc	1:0:5	NC	NC	NC	NC	NC
18.	Magnesium stearate	1:0:5	NC	NC	NC	NC	NC
19.	Lectose	1:2	NC	NC	NC	NC	*
20.	Drug+Placebo	1:5	NC	NC	NC	NC	NC
21.	Drug	--	NC	NC	NC	NC	NC

The Meaning of signs is mentioned below

NC = No change

* = Colour change with granule formulation

• = Formation of lumps

D:E = Drug: Excipient ratio

Table No. 2 : Preformulation Study of Dicloxacillin Sodium

S.NO	Excipients	D:E Ratio	Initial	25°C/60%RH		40°C/75RH	
				2nd week	4th week	2nd week	4th week
1.	Ethyl cellulose	1:0.5	NC	NC	NC	NC	NC
2.	Hydroxypropyl Mthyl cellulose	1:1	NC	NC	NC	•	•
3.	Croscarmellose Sodium	1:1	NC	NC	NC	NC	NC
4.	Microcrystalline	1:1	NC	NC	NC	NC	NC
5.	Starch	1:2	NC	NC	NC	NC	NC
6.	Pregelatinized starch	1:1	NC	NC	NC	NC	NC
7.	Sunset yellow supra	1:0:2	NC	NC	NC	NC	NC
8.	Sunset yellow lake	1:0:2	NC	NC	•	•	•
9.	Sodium lauryl sulphate	1:0:5	NC	NC	NC	•	•
10.	Aspartame	1:0:2	NC	NC	NC	NC	NC
11.	Saccharin Sodium	1:2	NC	NC	NC	NC	NC
12.	Sucrose	1:5	NC	NC	NC	*	*
13.	Golden Caramel	1:0:2	NC	*	*	*	*
14.	Orange dry flavour	1:0:2	NC	NC	NC	NC	NC
15.	Pineapple dry flavour	1:0:2	NC	NC	NC	NC	NC
16.	Colloidal silicon dioxide	1:1	NC	NC	NC	NC	NC
17.	Talc	1:0:5	NC	NC	NC	NC	NC
18.	Magnesium stearate	1:0:5	NC	NC	NC	NC	NC
19.	Lectose	1:2	NC	NC	NC	NC	*
20.	Drug+Placebo	1:5	NC	NC	NC	NC	NC
21.	Drug	--	NC	NC	NC	NC	NC

The meaning of signs is mentioned as,NC=No Change, * = Colour change with granule formation,
•=Formation of lumps D:E.=Drug: Excipient ration ±

Table No. 3: Preformulation Study of amoxicillin Trihydrate and Dicloxacillin Sodium

S.NO	Excipients	D:E Ratio	Initial	25°C/60%RH		40°C/75RH	
				2nd week	4th week	2nd week	4th week
1.	Ethyl cellulose	1:0.5	NC	NC	NC	NC	NC
2.	Hydroxypropyl Mthyl cellulose	1:1	NC	NC	•	•	•
3.	Croscarmellose Sodium	1:1	NC	NC	NC	NC	NC
4.	Microcrystalline	1:10	NC	NC	NC	NC	NC
5.	Starch	1:2	NC	NC	NC	NC	NC
6.	Pregelatinized starch	1:1	NC	NC	NC	NC	NC
7.	Sunset yellow supra	1:0:2	NC	NC	NC	NC	NC
8.	Sunset yellow lake	1:0:2	NC	NC	•	•	•
9.	Sodium lauryl sulphate	1:0:5	NC	NC	NC	•	•
10.	Aspartame	1:0:2	NC	NC	NC	NC	NC
11.	Saccharin Sodium	1:2	NC	NC	NC	NC	NC
12.	Sucrose	1:5	NC	NC	NC	*	*
13.	Golden Caramel	1:0:2	NC	*	*	*	*
14.	Orange dry flavour	1:0:2	NC	NC	NC	NC	NC
15.	Pineapple dry flavour	1:0:2	NC	NC	NC	NC	NC
16.	Colloidal silicon dioxide	1:1	NC	NC	NC	NC	NC
17.	Talc	1:0:5	NC	NC	NC	NC	NC
18.	Magnesium stearate	1:0:5	NC	NC	NC	NC	NC
19.	Lectose	1:2	NC	NC	NC	NC	*
20.	Drug+Placebo	1:5	NC	NC	NC	NC	NC
21.	Drug	--	NC	NC	NC	NC	NC

The meaning of signs is mentioned as, NC=No change, *=Colour change with granule formation
•=Formation of lumps, D:E.=Drug: Excipient ratio

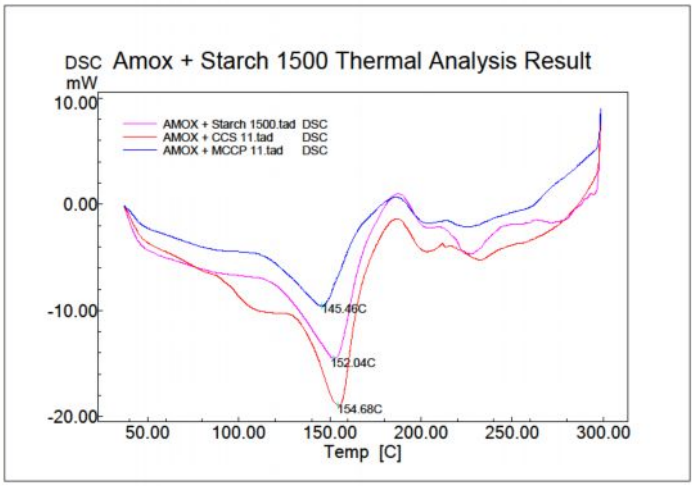

Fig: 1:DSC Thermogram for Amoxicillin trihydrate and excipients (starch 1500, Croscarmellose Sodium and Microcrystalline cellulose)

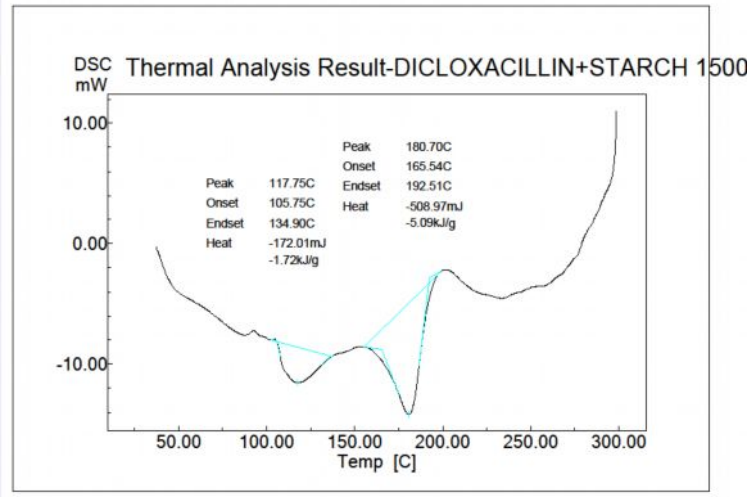

Fig :2: DSC Thermogram for Dicloxacillin and Starch 1500

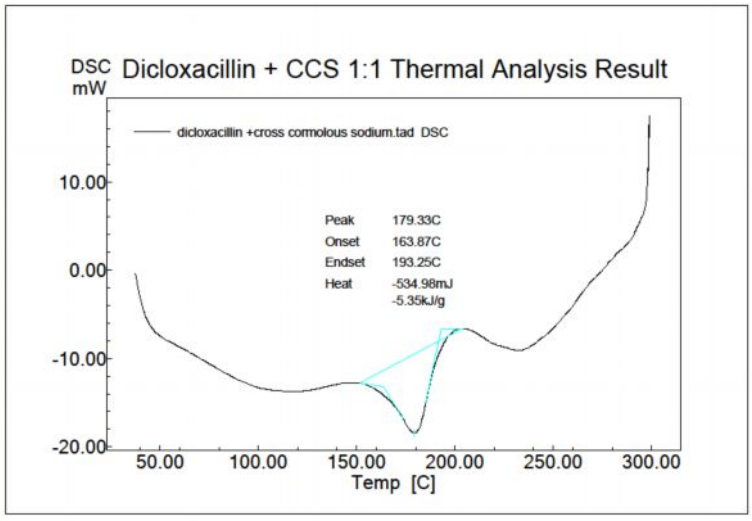

Fig :3: DSC Thermogram for Dicloxacillin and Croscarmellose Sodium

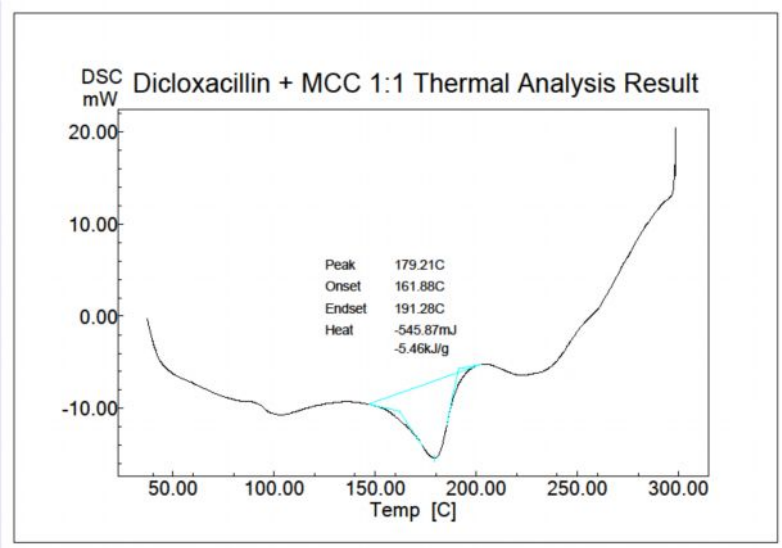

Fig :4: DSC Thermogram for Dicloxacillin and Microcrystalline cellulose

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