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FORMULATION AND *INVITRO* EVALUATION OF APREMILAST CONTROLLED RELEASE TABLETS

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ABSTRACT

The aim of the present research work is to formulate and evaluate controlled release matrix tablet of Apremilast by direct compression method using various polymers such as Xanthan gum, Sodium CMC, HPMCK4M and Ethyl cellulose. The present research project aimed to develop a control release oral formulation of antiviral drug Apremilast, useful for the treatment of chronic hyperuricemia and gout. Polymers like Xanthan gum, Ethyl cellulose, HPMC K4M, Sodium CMC were used for controlling the drug release and the polymers are mixed in a predetermined ratio. Selection of drug candidate, excipients and appropriate biocompatible polymers through preformulation studies including development of suitable analytical methods. Total 9 formulations were prepared, among the all 9 formulations, based upon the *invitro* studies F6 formulation containing 18% of Xanthan gum choosen as optimized formulation. So the drug release kinetics was performed for the F6 formulation.

Keywords: Apremilast, Xanthangum, Ethylcellulose, Sodium CMC and PVPK30.

INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage forms. Oral route is considered most natural, convenient and safe due to its ease of administration, patient acceptance and cost effective manufacturing process. Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption[1-3].

These immediate release dosage forms have some limitations such as drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance. Atypical peak-valley plasma concentration time profile is obtained which makes attainment of steady state condition difficult. The un-avoidable fluctuations in the drug concentration may lead to under medication or overmedication as the Css values fall or rise beyond the therapeutic range. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever over medication occurs[4-8].

Dosage forms which can reduce atleast a twofold reduction in dosing frequency as compared to the drug presented in a conventional form, such as solution or a prompt-releasing conventional solid dosage form are termed as extended release dosage forms. These products are formulated to make the contained medicament available over an extended period of time after administration within its therapeutic range and hence reduction in dosing frequency as compared to the conventional dosage forms. Modified-release products can also be explained by other different terms such as extended-release, prolonged-release, controlled-release, controlled-delivery, slow-release and sustained-release, delayed release, time release etc[9-12]. These formulations, by definition, have a reduced rate of release of active substance. In general, these terms are interchangeable. Delayed-release products are modified-release, but by definition is not extended-release. They can release discrete

amount (s) of drug some time after drug administration, e.g. enteric coated products exhibit a lag time during which little or no absorption occurs. While a number of such modified-release products are available as both prescription and over-the-counter drugs. Only a limited number have been shown to offer a therapeutic advantage.

MATERIALS AND METHODS

Apremilast were procured from B.M.R Chemicals, Hyderabad. Xanthan gum, Ethyl cellulose, Sodium CMC, PVPK30, Magnesium stearate and Talc were procured from Loba Chemie Pvt. Ltd, Mumbai.

Preparation of Apremilast controlled release tablets

In this process the tablets are compressed directly from powder blends of active ingredient and suitable excipients, which will flow uniformly in to the die cavity and forms affirm compact.

Step 1

Weighed all the ingredients separately.

Step 2

The drug and the other excipients were passed through 40# sieve together and blended for 10minutes.

Step 3

The magnesium stearate was passed through 60# sieve and added to the blend of step2 and blended for 5minutes.

Step 4

Compressed the blend of step 3 into tablets by using 8.5mm, round punches. (Table 1)

Flow properties

Angle of repose

Angle of repose is determined as the maximum angle possible between the surface of the pile of the powder and horizontal plane. Fixed funnel method was used to determine the angle of repose of powder or granules.

Bulk density

Weighed amount of the powder blend was taken and transferred to a measuring cylinder. Bulk volume of the blend is noted as per the reading on the measuring cylinder.

Tapped density

Tapped density is determined by the weighed quantity of powder blend is poured into the graduated cylinder, which is then tapped for 100 taps.

Compressibility Index

Compressibility index is important to measure the tendency of powder formulation. It indicates the flow properties of the blend. Low percentage of compressibility index indicates free flowing powder, whereas high compressibility index indicates poor flowing powder. (Table 2 and Table 3)

Evaluation of Apremilast controlled release matrix Tablets

***InVitro* Dissolution Studies**

From the *invitro* drug release studies of Apremilast controlled release tablets using Xanthan gum, Ethyl cellulose, Sodium CMC, in three different polymer ratios using MCC as a filler and PVPK30 as binder. Among the all 9 trails, F1-F3 trails were formulated using Ethyl cellulose in three different ratios like 6%, 12% and 18%, the drug release was decreased with increase in the polymer concentration. F1 formulation containing 6% of Ethyl cellulose shows 89.09% of drug release at the end of 24 hours, while F2 formulation containing 12% of Ethyl cellulose shows 90.28% of drug release at the end of 24 hours, whereas F6 formulation containing 18% of Ethyl cellulose shows 94.15% of drug release at the end of 24 hours. Further formulations were prepared using Xanthan gum. Then F4-F6 trails were formulated using Xanthan gum in four different ratios like 6%, 12%,18% and 24%. F4 formulation containing 6% of Xanthan gum shows 95.57% of drug release at the end of 24 hours, while F5 formulation containing 12% of Xanthan gum shows 97.82%of drug release at the end of 24hours,where as F6 formulation containing 18% of Xanthum gum shows 99.86% of drug release at the end of 16 hours. Further formulations were prepared using Sodium CMC. The *invitro* release profiles were shown in Figure 1.

FT-IR STUDIES

The IR spectrum of pure drug was found to be similar to the standard spectrum of Apremilast. From the spectra of Apremilast, combination of Apremilast with polymers, it was observed that all characteristic peaks of Apremilast were not altered and present without alteration in the combination spectrum, thus indicating compatibility of the drug and polymers. FT-IR spectra of Apremilast and optimized formulation are shown in Figure 2and 3 respectively.

RESULTS AND DISCUSSION

From the *invitro* drug release studies of Apremilast controlled release tablets using Xanthan gum, Ethylcellulose and Sodium CMC in three different polymer ratios using MCC as

a filler and PVPK30 as binder.

Among the all 9 trails, F1-F3 trails were formulated using Ethyl cellulose in three different ratios like 6%, 12% and 18%, the drug release was decreased with increase in the polymer concentration. F1 formulation containing 6% of Ethyl cellulose shows 89.09% of drug release at the end of 24 hours, while F2 formulation containing 12% of Ethyl cellulose shows 90.28% of drug release at the end of 24 hours, whereas F6 formulation containing 18% of Ethyl cellulose shows 94.15% of drug release at the end of 24 hours. Further formulations were prepared using Xanthan gum.

Then F4-F6 trails were formulated using Xanthan gum in four different ratios like 6%, 12%,18% and 24%. F4 formulation containing 6% of Xanthan gum shows 95.57% of drug release at the end of 24 hours, while F5 formulation containing 12% of Xanthan gum shows 97.82%of drug release at the end of 24 hours, whereas F6 formulation containing 18% of Xanthan gum shows 99.86% of drug release at the end of 16 hours. Further formulations were prepared using Sodium CMC.

Then F7-F9 trails were formulated using Sodium CMC in four different ratios like 6%, 12%, 18% and 24%. F7 formulation containing 6% of Sodium CMC shows 83.58% of drug release at the end of 24 hours, while F8 formulation containing 12% of Sodium CMC shows 86.47% of drug release at the end of 24 hours, whereas F9 formulation containing 18% of Sodium CMC shows 88.22% of drug release at the end of 24hours.

CONCLUSION

The studies showed of Apremilast controlled release tablets using Xanthan gum, Ethyl cellulose and Sodium CMC in three different polymer ratios using MCC as a filler and PVPK30 as binder. Among the all 9 formulations, based upon the *invitro* studies F6 formulation containing 18% of Xanthan gum choosen as optimized formulation. So the drug release kinetics was performed for the F6 formulation. Further it was subjected to pharmacokinectic studies.

Table 1: Formulation of Apremilast controlled release tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Apremilast	250	250	250	250	250	250	250	250	250
Ethyl cellulose	30	60	90	_	_	_	_	_	_
Xanthan gum	_	_	_	30	60	90	_	_	_
Sodium CMC	_	_	_	_	_	_	30	60	90
MCC	196	166	136	196	166	136	196	166	136
PVPK30	20	20	20	20	20	20	20	20	20
Talc	2	2	2	2	2	2	2	2	2
Mag. stearate	2	2	2	2	2	2	2	2	2
Total(mg)	500	500	500	500	500	500	500	500	500

Table 2: Pre Compression Parameters of Apremilast controlled release matrixTablets

FC	Angle of Repose	Bulk density	Tapped density	Hausners ratio	Carrs index
F1	28.84	0.335	0.324	1.13	12.85
F2	26.46	0.297	0.356	1.15	15.31
F3	29.47	0.306	0.335	1.18	11.56
F4	27.53	0.295	0.328	1.19	14.92
F5	28.66	0.339	0.389	1.13	15.45
F6	26.88	0.348	0.363	1.12	11.96
F7	27.65	0.314	0.395	1.18	12.85
F8	28.77	0.325	0.387	1.16	13.73
F9	29.23	0.328	0.338	1.14	12.57

Table 3: Physical properties of tablet formulation (F-1toF-9)

FC	Avg.Wt(mg)	Thickness(mm)	Hardness(kg/cm2)	Friability (%)	Drug Content (%)
F1	576.4	3.21	9.4	0.35	93.26
F2	583.2	3.27	8.2	0.61	89.68
F3	589.5	3.44	7.3	0.75	90.52
F4	584.02	3.12	6.9	0.62	97.66
F5	578.9	3.23	9.8	0.81	93.15
F6	585.03	3.28	7.4	0.73	91.81
F7	584.8	3.11	6.7	0.58	96.35
F8	586.4	3.46	8.9	0.82	98.62
F9	591.5	3.40	7.6	0.69	94.88

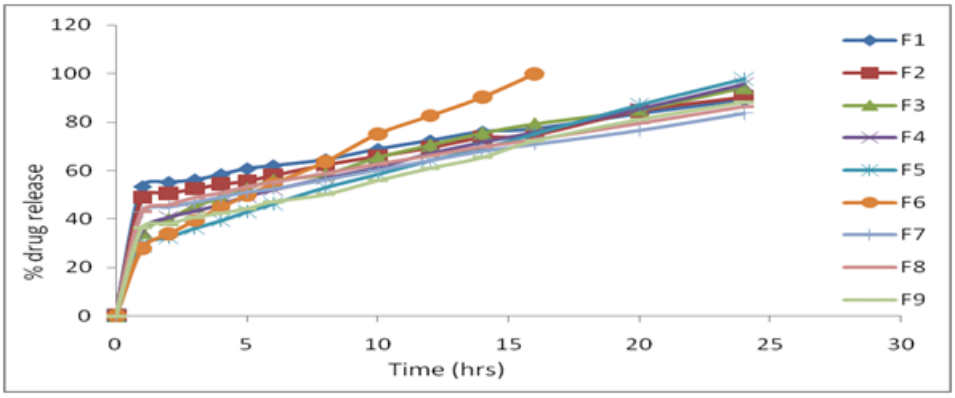

Fig. 1: *Invitro* dissolution data of formulations

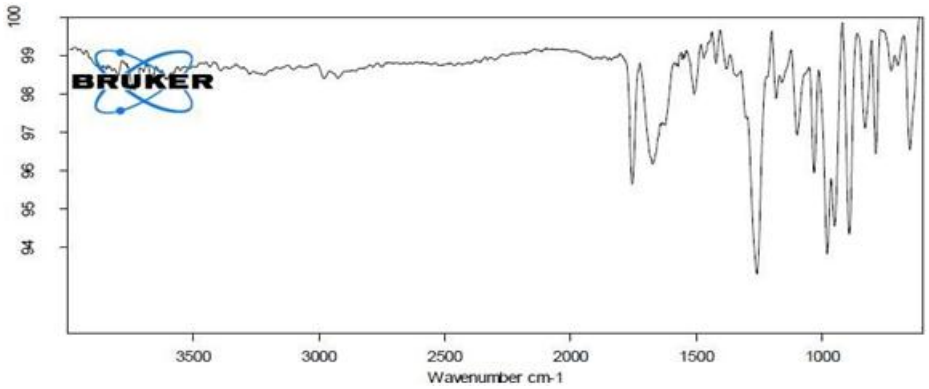

Fig. 2: FT-IR spectrum of Apremilast

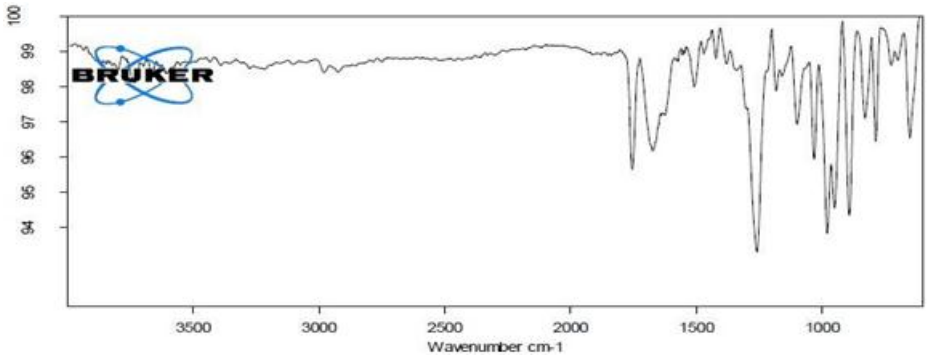

Fig. 3: FT-IR spectrum of optimized formulation

REFERENCES

1. Goodman and Gilman's the pharmacological basis of therapeutics, 10thedition, 2001: 991-992, 1758-1760.
2. Modern pharmaceutics, revised and expanded, edited by Gilbert S banker and Christopher T Rhodes. 2002.
3. Chein YW. Oral Drug delivery and delivery systems. In: Novel drug

delivery systems. Marcel Dekker, Inc., New York. 2002;50:3rd edition:139-196.
4. Brahmankar DM and Jaiswal SB. Biopharmaceutics and pharmacokinetics a treatise"1sted. Vallabh prakashan; New Delhi. 1995;64-70.
5. Vyas SP and Khar RK. Controlled Drug Delivery. Concepts and Advances, ed. 2002;155-195.
6. Sallsa T, Veiga F and Pina ME. Oral controlled –release dosage forms cellulose ether polymers in hydrophilic-matrices. Drug Development and Industrial Pharmcy.1997;23:929-938.
7. Gohel MC, Patel TP and Barigya SH. Studies in preparation and evaluation of pH independent sustained-release matrix tablets of Verapamil Hcl using directly compressible Eudragits. Pharamaceutical Development and Technology. 2003;8:323-333.
8. Liv J, Zhang F and McGinity Jw. Properties of lipophilic matrix tablets containing phenyl propanolamine hydrochloride prepared by hot-met extrusion. European Journal of Pharmaceutics and Biopharmaceutics. 2001;42:181–190.
9. GennaroAR. Extended Release Dosage Forms. In: Remington: The Science and Practice of Pharmacy. Lippincott Williams and Wilkins, U.S.A. 2000;1:20 th edition:660-63.
10. Liberman AH, Lachmann L and Joseph BS. Pharmaceutical Dosage Forms. Tablets. 3: 2ndEdition: 201-206.
11. Gilbert S, Banker, Christopher T and Rhodes. Modern Pharmaceutical 3rd Edition. 576-578.
12. Gurpreet A, Karan M, Inderbir S, Sandeep A and Vikas R. Formulation and evaluation of controlled release matrix mucoadhesive tablets of Domperidone using salvia plebeian gum. Journal of Advanced Pharmaceutical Technology and Research. 2011;2(3):163-169.