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Journal of Chemical and Pharmaceutical Research

J. Chem. Pharm. Res., 2010, 2(4):232-239

ISSN No: 0975-7384
CODEN(USA): JCPRC5

Effect of SAGO starch on Controlled release Matrix tablets of Tramadol HCL

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ABSTRACT

The present work was aimed to evaluate SAGO starch in controlled release matrix tablets of Tramadol HCL to optimize the release of the drug for 12 hrs to act as twice daily formulations. Controlled release polymer, HPMC (K4M) was used in the ratio of 3:1 to the drug. High concentration of the polymer is intentionally used keeping the swelling power and gel forming ability HPMC. Matrix tablets, TS-1 to TS-6 were prepared using wet granulation technique with 5% corn starch as granulating agent and 0, 5%, 10%, 15%, 20% and 25% of SAGO starch to the drug. The prepared tablets were evaluated for tabletting characteristics like weight variation, hardness, friability and drug content uniformity, and found that they were within the compendial limits. It is found that the SAGO starch enhanced the drug release from prepared controlled release formulations proportional to the concentration used in tablets. TS-4 was found to be the optimized formulation which has a release of more than 94.58% in 12 hrs having 15% SAGO. The release kinetics of the optimized formulation indicates that it has zero order release with erosion mechanism.

Key Words: Tramadol HCL, SAGO, Controlled release, HPMC, matrix tablets.

INTRODUCTION

In the design of oral controlled release formulations matrix system is the frequently used drug delivery system because of less risk involved in dumping a large dose, reproducibility, simplicity

of preparation and less variation. Polymers are suitable as matrix carriers, swellability of some polymers offer several advantages in design of pharmaceutical dosage forms. HPMC (K4M) is one frequently used hydrophilic polymer in the controlled release. The disruption of the polymer matrix will determine the rate of drug release from such polymers. Excipients used often influence these matrices and modulate the drug release[1-7]. Hence the interaction of SAGO starch polysaccharides on the HPMC matrices is studied in the present work to optimize the drug release for 12 hrs.

SAGO is a starch extracted from the pith of SAGO palm stems, *Metroxylon sagu*[8] (fam: palmae). The SAGO palm is felled, the trunk is split lengthwise and the pith is removed, the pith is crushed to release the starch, washed and strained to extract the starch from the fibrous residue.

Metroxylon sagu

Normal size of SAGO Starch procured from the market

SAGO starch is mixed with boiling water to form a paste and used as a thickener in dishes. SAGO starch is not just limited to its uses for the food industry, but can also be used as a key material input in various industries such as paper, plywood, and textile industry. SAGO starch is used to make adhesives, paper, ethanol, high fructose glucose syrup, maltodextrin and cyclodextrins. Because many starches and their derivatives were used in pharmaceutical dosage forms, the present investigation done to evaluate SAGO starch in its ability to control the release of Tramadol HCL from matrix tablets.

Tramadol HCL is a white or almost white, crystalline powder, freely soluble in water and in methanol, very slightly soluble in acetone. It is a centrally-acting analgesic[9-15], used for treating moderate to moderately severe pain. Tramadol HCL is used as drug of choice in this study because of its high solubility and less Biological half life. The drug is taken 4-6 times a day depending on requirement and hence it is felt appropriate to prepare and evaluate twice daily formulations of the drug.

EXPERIMENTAL SECTION

Materials

Tramadol HCL was procured as a gift sample from Tini Pharmaceuticals Ltd, Tirupati, India. SAGO was purchased from local market and is of food grade. HPMC K4M was supplied by Loba chemie, Mumbai, India. Magnesium stearate and talc were of S.D fine chemicals LTD, Mumbai, India and they are of laboratory grade.

Method

Preparation of SAGO tablets of Tramadol HCL:

The drug, ingredients and different proportions of SAGO passed through sieve no. 100 were weighed for a batch of 100 tablets as shown in Table 1 and thoroughly mixed using geometric dilution technique to ensure complete mixing and granulated with 5% corn starch. The wet granules were dried in a hot air oven below 50^{o} C until moisture content of granules reached between 2-3%. Tablets containing Tramadol HCL equivalent to 50 mg were compressed using 9 mm slightly concave round punches embossed with letters of SDC on 16 station rotary compression machine. Compression force of the machine was adjusted to obtain hardness in the range of 4-5 Kg /cm^2.

Table 1: Composition of SAGO based tablets of Tramadol HCL

Ingredients (mg per tablet)	Formulation code					
	TS-1	**TS-2**	**TS-3**	**TS-4**	**TS-5**	**TS-6**
TRAMADOL HCL	**50**	**50**	**50**	**50**	**50**	**50**
SAGO	**0**	**2.5**	**5**	**7.5**	**10**	**12.5**
5% Corn starch equivalent to	**05**	**05**	**05**	**05**	**05**	**05**
HPMC 100 K4M	**150**	**150**	**150**	**150**	**150**	**150**
Magnesium stearate	**7**	**7**	**7**	**7**	**7**	**7**
Talc	**3**	**3**	**3**	**3**	**3**	**3**
Tablet weight (mg)	**215**	**217.5**	**220**	**222.5**	**225**	**227.5**

Evaluation of prepared matrix tablets:

All the prepared formulations were evaluated for Hardness, Weight variation, Friability and Drug content uniformity, all the prepared tablets were found to be within the compendial limits and the results are as given in Table 2.

Table 2: Tabletting characteristics of SAGO based tablets of Tramadol HCL

Formulation	Weight[a] (mg)	Drug content[b] (%)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)
TS-1	214.2 ± 1.32	99.58 ± 0.88	4-5	1.4	0.34
TS-2	218.4 ± 2.11	98.95 ± 1.08	4-5	1.5	0.29
TS-3	221.3± 1.64	99.19 ± 1.54	4-5	1.8	0.49
TS-4	223.4 ± 2.04	99.66 ± 1.27	4-5	2.0	0.32
TS-5	226.8 ± 1.12	98.33 ± 1.17	4-5	2.2	0.37
TS-6	228.2±1.24	99.73±1.16	4.5	2.3	0.48

a: Mean ± s.d., n = 20 tablets; b: Mean ± s.d., n = 10 tablets

Dissolution test was carried out using USP type-II (Paddle) dissolution test apparatus of Model DISSO 2000 of M/s. Lab India at a stirring rate of 50 rpm. 900ml of distilled water is used dissolution medium maintained at 37 ± 0.5° C. 5 ml of sample volume was withdrawn periodically, appropriately diluted and analyzed using Systronics UV-Visible Spectrophometer (117) at 271 nm. The 5 ml of volume maintained at the temperature of the dissolution basket was replaced after each sampling. Cumulative % drug released of all the formulations TS-1 to TS-6 was as shown in Fig. 1. The comparative cumulative % of the TS-4 and commercial was given in Fig. 2. The data is fitted to popular kinetic equations, Zero order, First order, Erosion and Higuchi. The linear regression plots were given in Fig. 3.

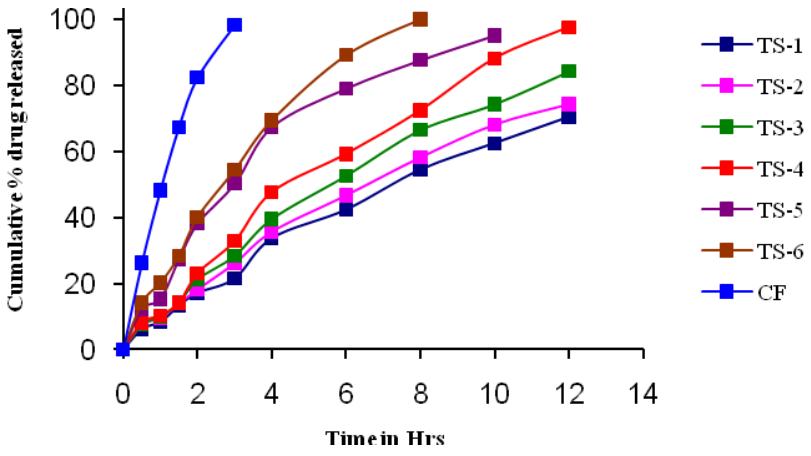


Fig. 1: Cumulative % drug released from all the formulations TS-I to TS-6

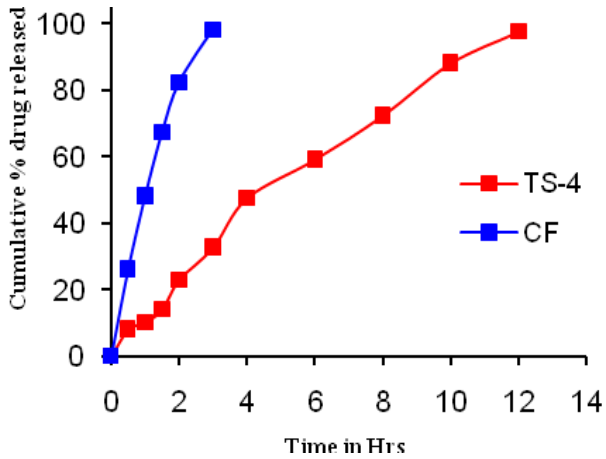
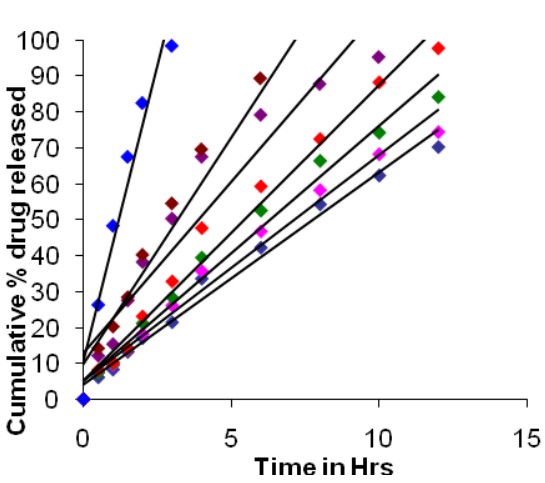
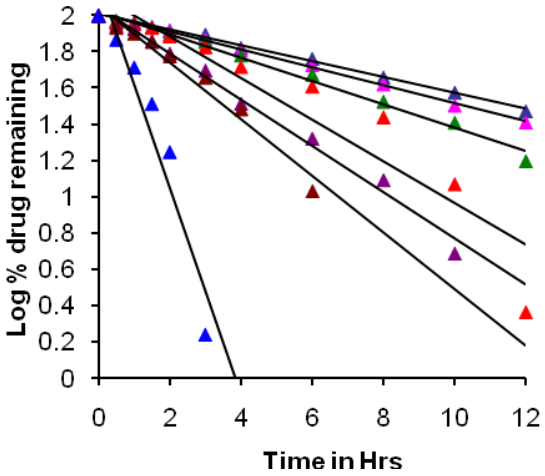


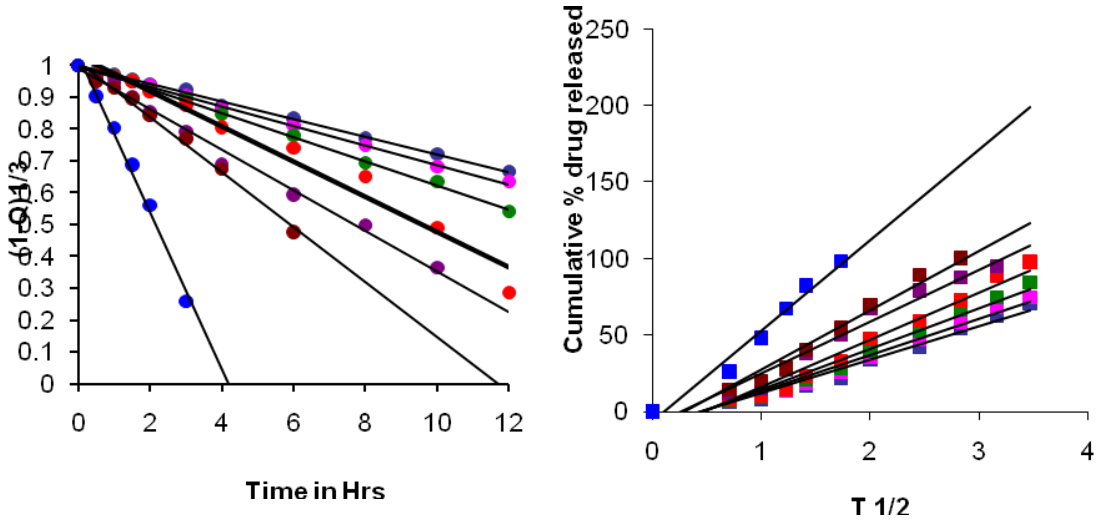
Fig. 2: Cumulative % drug released from commercial and optimized formulation TS-4



Zero order



First order



Erosion Higuchi

Fig. 3: Linear regression plots of prepared matrix tablets of TS-I to TS-6

RESULTS AND DISCUSSION

Different formulations were prepared as per the composition given in Table 1. The prepared formulations TS-1, TS-2, TS-3, TS-4, TS-5, TS-6 were evaluated for drug content variation, friability, weight variation, hardness, thickness.

The drug content of all the combinations was found to be within the limit and it is satisfactory. The low s.d values of the formulation indicate their drug content uniformity. Hence, there is no batch to batch variation among the formulation. All the tablets were found to have good tablet thickness ratio and hardness to with stand the handling abrasion. The friability of all the formulations is less than 1 percent as given in the Table 1. All the formulations thus are with enough ability to with stand the pressure, stress, friction during the transportation.

The dissolution profiles of all the formulations were carried out in U.S.P-II type apparatus. Formulation TS-1 could able to release 70% of Tramadol HCL by the end of 12 hours. The primary objective of present study is to prepare a formulation of Tramadol HCL which can able to release 100% drug in 12 hours.

In order to achieve a formulation which can release drug up to 12 hrs different ratios of ‘SAGO starch’ were added in formulations TS-2 to TS-6. Starch is a well known diluent and disintegrant. Hence, in the present study SAGO as alternative source to starch is tried and its ability to act as disintegrant is evaluated. TS-2 formulation contains 5 % of SAGO to that of the drug similarly TS-3 with 10%, TS-4 with 15%, TS-5 with 20% and TS-6 with 25%. The addition of disintegrant in these formulations increased the drug release, due to the following mechanism.

The HPMC is a Hydrophilic Polymer which when comes in contact with water forms a gel surrounding the tablet and acts as a barrier of control in the drug release from the tablets. The high concentration of HPMC in formulations TS-1 to TS-6 is intentionally used to control the release of highly soluble Tramadol HCL. SAGO acts a channeling agent and makes pores in the gel barrier or in the matrix making ways to the drug molecule to come out and thereby increasing the drug release.

In formulation TS-1 there is no starch and hence the HPMC affectively controlled the drug release beyond 12 hours. Where as in TS-2 5 % of SAGO could able to increase release and hence 74.36% of drug was released which is higher than the TS-1 release at the same time. TS-3 showed further release due to increase in concentration of SAGO in the formulation 84.27 % was released by the end of 12 Hours. However, 100 % of Drug is released in 12 hours when 15 % of SAGO is used in the formulation. Hence, this formulation is considered as optimized formulation. The formulation TS-5 released 100% of drug within 10 hours similarly TS-6 released 100% drug within 8 hours. This could be because of excessive disintegrating agent in these formulations. The mechanism of drug release from these formulations were calculated by fitting the data into popular models of drug release kinetics of Zero order, First order, Higuchi, Erosion mechanisms and their plots were given in Fig. 3. The formulations TS-1 and TS-5 showed regression value 0.998 and 0.994 respectively where as TS-2, TS-3, TS-4, TS-6 and commercial formulation showed regression values 0.999, 0.999, 0.998, 0.996 and 0.981 respectively. All the formulations including commercial formulation exhibited erosion mechanism. The optimized formulation was compared with commercially available immediate release dosage form Tramadol HCL which released 98.27% within 3 hours since there are no formulations with 12 hours release profile. The optimized formulation TS-4 is compared with commercial formulation of immediate release nature procured from the local market having trade name ULTRAM.

CONCLUSION

Synthetic substances were undoubtedly having harmful side effects, hence natural substances and natural excipients were gaining popularity. In this context the present work was selected to evaluate the excipient ability of SAGO, being a natural substance, food grade substance it is safe and free from any adverse events. In this study matrix tablets of Tramadol HCL were prepared using HPMC K4M and the formulations were optimized to release the drug for 12 hours to make twice daily formulation of Tramadol HCL using SAGO starch. 15% of SAGO starch successfully enhanced the drug release in TS-4 than in TS-1 to prepare twice daily formulation.

Hence, it can be concluded SAGO is an effective replacement for starch and can be used as desintegrant in the pharmaceutical dosage forms. It is safe effective and easily available hence it can be considered it is more useful than synthetic diluents and disintegrants having adverse effects.

Acknowledgements
The authors thank the management and the Principal of Sri Padmavathi School of Pharmacy, Tiruchanoor for their encouragement and providing facilities to carry out the work.

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