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Research Article

FORMULATION, EVALUATION AND COMPARISION OF DISSOLUTION PROFILES OF ESLICARBAZEPINE ACETATE IMMEDIATE RELEASE TABLETS USING NATURAL BINDERS AGAINST SYNTHETIC BINDER

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ABSTRACT

Objective: The objective of the present study was to formulate, evaluate and compare the dissolution profiles of Eslicarbazepine acetate (ESL) immediate release tablets using natural binders like tapioca starch, maize starch and galbanum, against the synthetic binder like Polyvinyl Pyrrolidone (PVP).

Methods: These natural binders were used as novel excipients which formed weak attractive bonds with the drug by complexation during wet granulation and increased the solubility of ESL. Each of these natural and synthetic binders was used separately in different concentrations to prepare immediate release tablets of ESL. Dissolution profiles of these tablets were compared.

Results: The in-vitro drug release of F4 (with galbanum 1%) was highest 98.78%, whereas the least drug release of 61.66% was shown by F12 (with PVP 3%).

Conclusion: It was seen that the tablets with natural binders showed better release characteristics in comparison to the tablets with synthetic binder PVP. Formulation with galbanum 1% showed best release profile. Galbanum also has antiepileptic property which can act synergistically with Eslicarbazepine acetate to treat seizures. It was also seen that among the various concentrations of binders used formulations with 1% binder showed better release characteristics when compared to 2% and 3%.

Keywords: Binders, Solubility, Novel, Dissolution, concentration

INTRODUCTION

Immediate release tablets are designed to disintegrate and release their medicaments with no special rate controlling features such as special coatings and other techniques. Immediate release dosage forms are most commonly formulated when the half life of the drug is more and there is no necessity of frequent dosing. This also serves as an advantage for patient compliance. Other reason for formulating immediate release dosage form is rapid response. [1]

In the present study, the API, Eslicarbazepine acetate is a pro-drug, which is metabolized to active form S-licarbazepine which is a potent form of the drug without any toxication, whereas oxcarbazepine forms both R and S form, the R form produces toxic metabolites. ESL has a half life of 13-20hrs, which means it is a suitable candidate for immediate release dosage form. It has almost complete bioavailability. [2, 3]

Novel excipients are used which enhance the solubility of poorly soluble drug Eslicarbazepine acetate by forming complexes with them. The mechanism by which it improves solubility is more closely related to complexation involving a weak interaction between the novel excipient and the poorly soluble drugs. It is a solubilization process, whereby addition of a large amount of second water soluble solute, results in an increase in the aqueous solubility of first solute. The starches used, also have a good disintegrating property. When the mucilage is prepared, starch converts into glucose and dextrin. [4, 5]

The Natural Binders were used in three different concentrations 1%, 2%, 3% to formulate immediate release tablets of Eslicarbazepine acetate using wet granulation technique. The synthetic binder PVP was also used in three different concentrations 1%, 2%, 3%. 12 different formulations of immediate release dosage form were prepared.

MATERIALS AND METHODS

Materials

Eslicarbazepine acetate was obtained as a gift sample from Ami life sciences Pvt. Ltd. CrossCarmellose sodium; PVP K 30 was obtained from Yarrow Chem. Products, Mumbai, Tapioca starch and maize starch was obtained from Surya min chem., Magnesium stearate, Talc was obtained from Molychem. Galbanum was obtained from a local vendor.

Table 1: It shows formula for the preparation of immediate release tablets of Eslicarbazepine acetate

Formulation	Eslicarbazepine acetate	CCS (mg)	Tapioca starch	Maize starch	Galba-num	PVP	Magnesium Stearate	Talc
F1	200mg	10	1%	-	-	-	4mg	6mg
F2	200mg	10	2%	-	-	-	4mg	6mg
F3	200mg	10	3%	-	-	-	4mg	6mg
F4	200mg	10	-	1%	-	-	4mg	6mg
F5	200mg	10	-	2%	-	-	4mg	6mg
F6	200mg	10	-	3%	-	-	4mg	6mg
F7	200mg	10	-	-	1%	-	4mg	6mg
F8	200mg	10	-	-	2%	-	4mg	6mg
F9	200mg	10	-	-	3%	-	4mg	6mg
F10	200mg	10	-	-	-	1%	4mg	6mg
F11	200mg	10	-	-	-	2%	4mg	6mg
F12	200mg	10	-	-	-	3%	4mg	6mg

Method of Preparation

Twelve different formulations of Eslicarbazepine acetate immediate release tablets are prepared using ingredients as given in Table no.1. Different concentrations of natural binders were used to prepare immediate release tablets of Eslicarbazepine by wet granulation method. Crosscarmellose sodium was used as a super disintegrant, Tapioca Starch, maize starch and galbanum were used as natural binders and PVP is used as a synthetic binder. Magnesium stearate was used as a lubricant and talc was used as a glidant.

Twelve different formulations of Eslicarbazepine acetate were prepared. The pure drug Eslicarbazepine acetate was mixed with Crosscarmellose sodium and the mixture was wet granulated using a natural or synthetic binder of different concentrations 1%, 2%, 3%. The granules were passed through sieve of mesh number 10. Then these granules were dried in a hot air oven at 60°C. The dried granules were passed through sieve of mesh number 22. The dried granules that passed through the 20 mesh sieve were lubricated with magnesium stearate and talc. This mixture was subjected to different pre formulation studies namely Bulk density, Tapped Density and Angle of Repose, compressibility index and Hausner's ratio. Finally the dried granules were compressed as tablets by Mini-Press compression machine.

RESULTS AND DISCUSSION

Pre-Compression characterization of API and granules:

The compatibility of drug and each excipient was studied using FT-IR. It was found that there was no interaction between any excipient and the drug. The lubricated powder blend was evaluated for density parameters like bulk density, tapped density, compressibility index and Hausner's ratio was calculated to estimate the flow properties.

Table 2: It shows pre-compression characterization of API and dried granules

Formulation Code	Bulk density (g/ml)	Tapped density (g/ml)	Angle of Repose (°)	Carr's Index (%)	Hausner Ratio
API	0.528	0.628	28.8	15.9	1.18
F1	0.512	0.600	27.6	14.6	1.17
F2	0.520	0.610	28.98	14.7	1.17
F3	0.488	0.610	29.68	20	1.25
F4	0.50	0.590	29.03	15.2	1.18
F6	0.492	0.600	29.07	18	1.21
F7	0.484	0.576	27.42	15.9	1.19
F8	0.492	0.600	29.55	18	1.21
F9	0.496	0.590	27.44	15.9	1.18
F10	0.48	0.57	28.05	15.9	1.18
F11	0.476	0.58	27.9	17.9	1.21
F12	0.48	0.585	29.16	17.9	1.21

Post Compression characterization of tablets

Post compression characterization of tablets was carried out by testing their hardness, friability, uniformity of weight, thickness, wetting time, disintegration time and drug content.

The *in-vitro* dissolution studies were performed for the twelve formulations to evaluate the dissolution characteristic of Eslicarbazepine acetate tablets in the presence of Binders used as novel excipients. Also the dissolution profiles of all the formulations were compared and the optimized formulation among them was selected. The results are presented in Table No.4. The dissolution study of all the formulation was found to be F1-95.04%, F2-92.23%, F3-90.81%, F4-88.69%, F5-84.08%, F6-81.3%, F7-98.78%, F8-94.22, F9-91.41%, F10-68.91%, F11-64.47%, F12-61.66%. Among all the formulations F7 shows the best release profile when compared to other eleven formulations. Also it was observed that the release profile of tablets with natural binders have better release characteristics when compared to tablets with synthetic binder. Among the natural excipients used, galbanum showed the properties of a novel excipient which when used in the formulation of tablet showed better drug release. Galbanum also has antiepileptic effect which can act synergistically with Eslicarbazepine acetate without producing any toxicity. Among the different concentrations of binders used 1% binder in all the formulations showed better release characteristic when compared to 2% and 3%. The results are given graphically in figure 1.

Table 3: It shows post-compression characterization of tablets

Parameter	Formulation											
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
Hardness (kg/cm$^{2)}$	4.9	4.3	4.5	4.5	4.6	4.8	4.2	4.3	4.5	4.1	4.3	4.5
Friability (%w/w)	0.3	0.22	0.37	0.15	0.22	0.30	0.22	0.30	0.30	0.37	0.30	0.37
Thickness (mm)	2.9	2.92	2.96	2.89	2.92	2.88	2.96	2.90	2.86	2.9	2.91	2.9
Diameter (mm)	4.9	4.88	4.96	4.98	4.89	4.93	4.91	4.97	4.94	4.95	4.88	4.9
Wetting time (Sec)	30	28	31	34	36	37	26	28	29	37	39	40
Weight Variation (mg)	222.1	221	220	221.3	219	220	220.5	221	219	221.3	222	223
In-Vitro Disintegration time (sec)	20.5	22	22.5	23.5	24	25	18	20	21	27	28	30
Drug Content (%)	97.04	96.32	95.89	97.7	98.1	97	99	97.2	96.3	92	92.1	93

Table 4: It shows *in-vitro* drug release of various formulations

Formulation	5	10	15	20	30	45	60
F1	26.6	44.78	53.23	65.37	77.37	90.68	95.04
F2	25.5	41.7	51.65	61.77	75.73	88.52	92.23
F3	22.93	36.98	48.38	58.68	70.60	87.58	90.81
F4	26.04	41.61	50.48	58.47	72.43	85.96	88.69
F5	25.09	37.8	47.56	55.66	71.56	80.78	84.08
F6	20.86	35.34	44.31	52.39	69.21	80.01	81.3
F7	31.77	48.1	57.3	70.60	80.31	93.5	98.78
F8	30.6	43.85	53.15	66.49	75.10	90.73	94.22
F9	28.69	40.66	49.06	61.69	72.70	88.41	91.41
F10	14.18	27.81	33.76	41.75	53.23	62.48	68.91
F11	12.68	25.96	31.41	38.61	50.80	60.87	64.47
F12	10.63	23.80	28.71	91.41	68.91	64.47	61.66

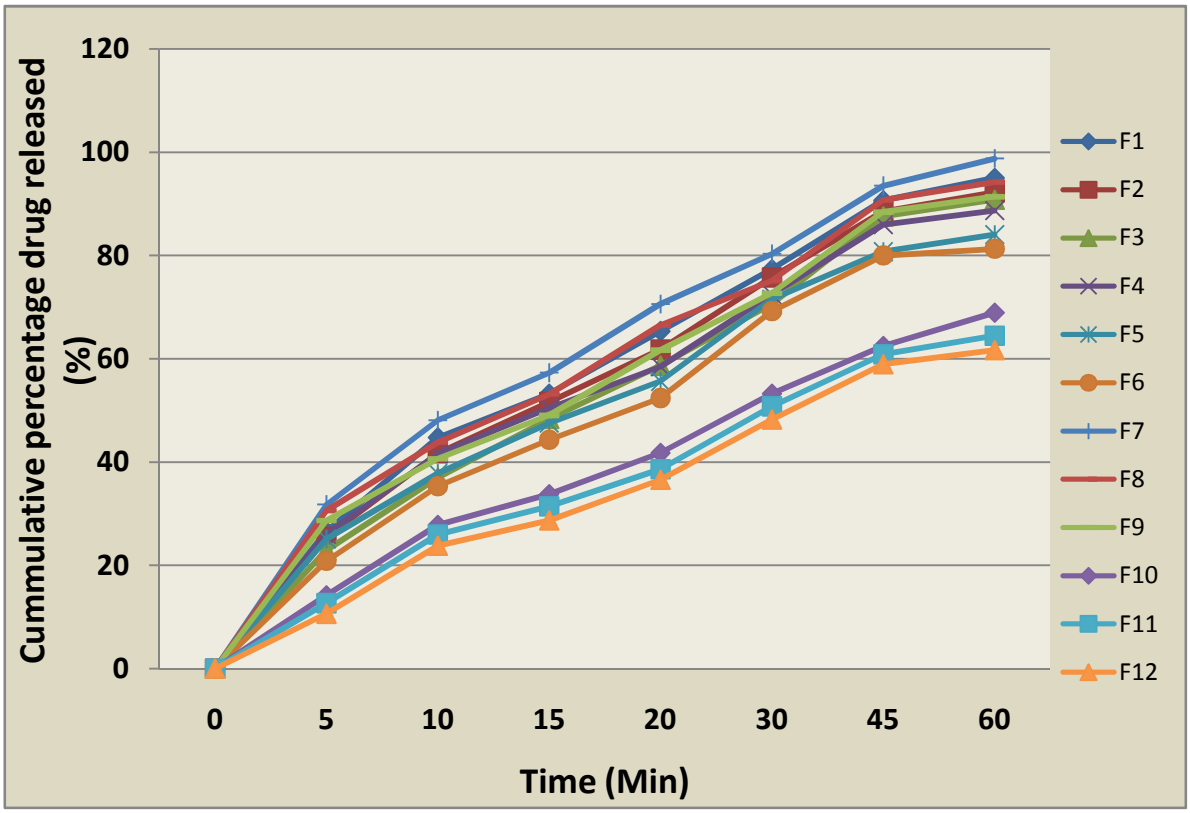

Fig. 1: It shows comparison of dissolution profiles of different formulations

The compressed tablets were characterized by their physical properties. The average tablet weight was determined for 20 tablets. Tablet hardness was tested using Monsanto tablet hardness tester. Friability of the tablets was determined by Roche friabilator. Tablet friability was calculated as the percentages of weight loss of 20 tablets after 100 rotations. The physical parameters of granules were provided in Table No. 2.

CONCLUSION

Immediate release tablets of Eslicarbazepine acetate was prepared by wet granulation method using various natural binders and a synthetic binder PVP. It was seen that the formulations with natural binders showed better release characteristics when compared to the formulations with synthetic binder PVP. Among the natural binders, galbanum showed the best dissolution profile and can be used successfully in future to prepare antiepileptic tablets because it has an optimum binding effect and also antiepileptic property. Among the various concentrations of binders used formulations with 1% binder showed better release characteristics when compared to 2% and 3%.

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