Research Article

PREPARATION AND *IN VITRO* EVALUATION OF TORSEMIDE MATRIX TABLETS USING DIFFERENT SODIUM ALGINATE GRADES

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ABSTRACT

The objective of this study was to design oral controlled release matrix tablets of torsemide using different viscosity grades of sodium alginates as release rate retardants. The study mainly focus on effect of various formulation factors such as polymer content, polymer type, and compression force on the *in vitro* release of drug. The *in vitro* drug release studies were performed using a USP Type II dissolution apparatus. The dissolution medium was 900 ml of 6.8 pH phosphate buffer for 16 h. The temperature of dissolution medium was maintained at 37°C ± 0.5°C. The data of dissolution were fitted to various kinetics models. *In vitro* release studies showed that the release rate decreased with increase in polymer concentration and viscosity of the polymer. The matrix tablets containing sodium alginate LF 5/60 was extended the drug release form 13 to 17 h. The matrix tablets containing sodium alginate LF 10/60 was extended the drug release form 10 to 14 h. The matrix tablets containing sodium alginate LF 240 D was extended the drug release form 11 to 17 h. The data of the release kinetics showed the first-order release with diffusion mechanism. The differential scanning calorimetry and Fourier-transform infrared study showed no drug-polymer interaction.

Key Words: Differential scanning calorimetry, Fourier-transform infrared, matrix tablets, sodium alginate, Torsemide

INTRODUCTION

Conventional dosage forms are the most preferred and convenient option for drug delivery. However, it has poor patient compliance with ensuing undesirable toxicity and poor efficiency. A major challenge thus lies in optimizing the properties of the drug and its delivery mechanism in producing safe and efficient drugs. Consequently, there is a need for new drug delivery systems and they represent one of the Frontier research areas.[1-3]

Torsemide is a new generation loops diuretic belonging to pyridine-sulfonylurea class and has been used for the treatment of both acute and chronic congestive heart failure, liver cirrhosis, and arterial hypertension. It exerts longer duration of action with a bioavailability of 80% and elimination half-life of 3-4 h compared with other loop diuretics.[4-9] The conventional formulation of Torsemide shows rapid absorption after oral administration which leads to high plasma concentration and fluctuations resulting more frequency of administration.[10] Hence, the need for the design and evaluation of the controlled

release formulation was critical. Torsemide controlled release tablets compared to immediate release has similar systemic exposure, but significantly reduces the rate of absorption and fluctuations in plasma concentrations thus offering a better tolerability.[11-13] The aim of this study is to design controlled release tablets of torsemide in a suitable polymer matrix thus enabling higher efficiency and better tolerability.

Objective

The main objective of the present work is to develop extended release matrix tablets of torsemide and to study the stability of the prepared formulations.

MATERIALS AND METHODS

Materials

Torsemide was obtained as a gift sample from Alkem Laboratories Ltd (Mumbai, India). Sodium alginate was obtained from FMC biopolymer, lactose (Pharmatose DCL 11) was obtained form DMV International, the Netherlands, colloidal silicon dioxide (Aerosil) was obtained form Degussa, Germany, talc was obtained form Luzenac, France, and magnesium stearate was obtained form Ferro Industrial Chemicals USA.

Methods

The matrix tablets of torsemide were prepared using different percentage concentrations of sodium alginate LF5/60. The drug, sodium alginate, and microcrystalline cellulose were directly mixed uniformly and the blend was added with aerosil and talc and finally lubricated with magnesium stearate. The concentration of sodium alginate LF5/60 used in the above formulations was 15%, 20%, and 25%. The tablets were compressed using 8 mm round-shaped punch, with cadmach rotary compression machine. The prepared matrix tablets were evaluated for various physicochemical properties. *In vitro* dissolution was performed USP Type I dissolution apparatus (LABINDIA, DISSO-2000,

Table 1: Physicochemical properties and release kinetics of the prepared matrix tablets of torsemide

Ingredients (mg)	mg/tablet								
	T-1	T-2	T-3	T-4	T-5	T-6	T-7	T-8	T-9
Torsemide	20	20	20	20	20	20	20	20	20
Sodium alginate LF5/60	15	20	25	*	*	*	*	*	*
Sodium alginate LF10/60	*	*	*	15	20	25	*	*	*
Sodium alginate LF 240D	*	*	*	*	*	*	15	20	25
Avicel Ph 200	55	50	45	55	50	45	55	50	45
Aerosil 200	5	5	5	5	5	5	5	5	5
Talc	4	4	4	4	4	4	4	4	4
Magnesium stearate	1	1	1	1	1	1	1	1	1
Total weight	100	100	100	100	100	100	100	100	100
Physical parameters									
Thickness (mm)	4.4	4.6	4.8	4.8	4.7	4.8	4.7	4.6	4.8
Hardness (kg/cm^2)	9	10.1	9.3	9.7	9.9	9.7	10	9	9
Weight variation (mg)	100	100	100	100	100	100	100	100	100
Friability (%)	0.5	0.6	0.6	0.3	0.2	0.4	0.3	0.3	0.1
Drug content (%)	99.78	99.17	101	99.87	99.56	99.11	99.34	99.56	99.15
Zero order	0.9219	0.9194	0.9344	0.9514	0.9456	0.9281	0.9447	0.9212	0.8913
First order	0.9533	0.9613	0.9622	0.9831	0.9826	0.9912	0.9825	0.9931	0.9947
Higuchi	0.9813	0.9828	0.9899	0.9831	0.9874	0.9861	0.9857	0.9907	0.9967
Peppas (n)	0.4085	0.4783	0.5111	0.4573	0.5461	0.6724	0.4741	0.5681	0.7001

Mumbai, India) at 100 rpm. The dissolution medium consisted of 900 ml of 0.1 N HCl for first 2 h and 6.8 pH phosphate buffer for the remaining period maintained at 37°C ± 0.5°C. An aliquot (5 mL) was withdrawn at specific time intervals and drug content was determined by UV-visible spectrophotometer (Schimadzu, UV-1700 E 23) at 263 nm. The release studies were conducted in triplicate. The Fourier-transform infrared (FT-IR) spectra acquired were taken from dried samples. An FT-IR (Thermo Nicolet 670) spectrometer was used for the analysis in the frequency range between 4000 and 400/cm, and 4/cm resolution. Differential scanning calorimetry (DSC) study of tablet was performed using a diamond DSC (Mettler Star SW 8.10) to determine the drug excepient compatibility study.

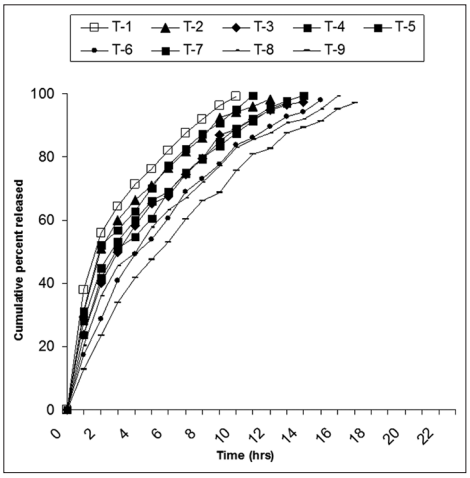

Figure 1: *In vitro* dissolution plot of the prepared torsemide matrix tablets

RESULTS AND DISCUSSION

All the torsemide matrix tablets with sodium alginate were evaluated for various physicochemical parameters such as weight variation, hardness, thickness, friability, and drug content. The hardness of the tablets was found in the range of 9-10 kg/cm^2. Friability below 1% clearly indicates the good mechanical strength of the prepared tablets. Assay of the prepared matrix tablets was found to in the range of 99-101% clearly indicates good content uniformity. The thickness of tablets was found in the range of 4.6 to 4.8 mm (Table 1). The weight variation of the tablets was with in the range and found to be 100 mg in all tablets. The dissolution study showed that the prepared matrix tablets with LF5/60 extended the drug release up to 14 h for the matrix tablets prepared with LF10/60 extended up to 16 h and for the matrix tablets prepared with LF240 D extended up to 17 h (Figure 1). The release kinetics was best fitted to first-order release with diffusion mechanism. DSC and FT-IR study showed no drug-polymer interaction (Figure 2).

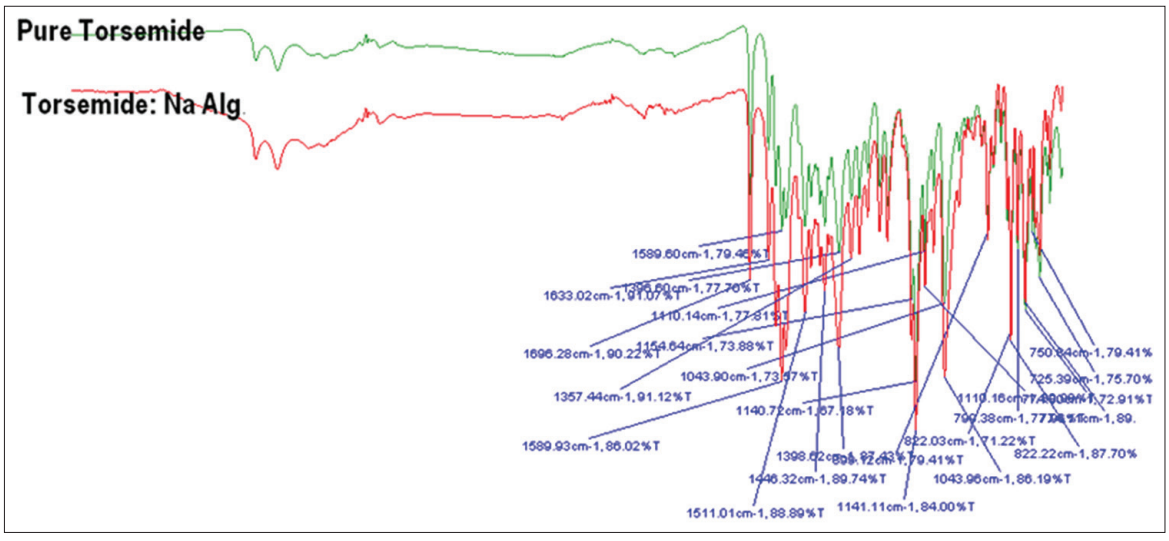

Figure 2: Fourier-transform infrared spectrum of pure torsemide and formulation

CONCLUSION

Matrix tablets of torsemide with different sodium alginates was prepared were showed good physicochemical properties and good prolonged release effect. The prepared matrix tablets were good stability. The prepared matrix tablets were good commercial applications.

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