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Formulation And Evaluation of Sustained Release Matrix Tablet of Pentoxifylline

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A B S T R A C T :

The goal of the current study was to create an extended-release pentoxifylline tablet for the management of peripheral vascular disease. Improved efficacy, fewer side effects, affordability, adjustable release properties, convenience, and patient compliance are some of the possible therapeutic advantages of a well-designed multilayered dosage form. Pentoxifylline is a haemorrhagic agent, or vasodilator. It functions by making it easier for blood to pass through constricted arteries. Restricted-release These tablets are multilayered, with a Pentoxifylline core layer encircled by barrier layers that could be composed of hydrophobic polymers like Hydroxy Ethyl cellulose (HEC for outermost layer) and hydrophilic swellable polymers like Hydroxypropyl Methylcellulose (HPMC K4 M for inner layer). Because HEC layers reduce the surface area available for Pentoxifylline to release or regulate the rate at which the solvent penetrates the layers, they delay and minimise the interaction between the gastrointestinal environment and the active core. By expanding the surface area and eventually releasing more Pentoxifylline. The medication core is coated using a traditional coating pan, and weight increases of 4%, 6%, and 8% of the overall tablet weight are to be achieved. Nine batches with different weight gains of both barrier polymers must thus be made. These batches will then be optimised for further characterisation using short-term stability experiments, swelling indices, and in vitro dissolution.

Keywords: Controlled release tablet, Sustained release tablet, Pentoxifylline, Matrix tablet

Introduction

The development of sustained or controlled release drug delivery systems has received more attention in the last 30 years due to the rising costs and challenges of marketing new drug entities and the corresponding recognition of the therapeutic benefits of controlled drug delivery. Reducing the frequency of dosing or increasing medication efficacy by localization at the site of action, lowering the amount needed, or ensuring uniform drug distribution are the objectives of building sustained or controlled drug delivery systems. The need for patient compliance dosage forms has increased during the last few decades. Consequently, there is now a threefold yearly growth in demand for the technology. Pharmaceutical firms are concentrating on developing novel drug delivery methods for current drugs with enhanced effectiveness and bioavailability together with a lower frequency of dose to minimize adverse effects because the development cost of new chemical entities is quite costly. Because of its systemic effects, oral medication administration is the most favoured and preferable way to provide therapeutic medicines. Furthermore, oral medications are typically regarded as the initial research route in the creation and discovery of novel pharmacological formulations and therapeutic substances, mostly due to their ease of administration and patient acceptability. It is widely accepted, accounting for 50–60% of all dose forms. Easy administration, precise dose, self-medication, avoiding discomfort, and—above all—patient compliance are the main reasons why solid dosage forms are so widely used. Tablets and capsules are the most often used solid dose forms.(9).Pentoxifylline is a prescription drug used to improve the symptoms of a certain blood flow problem in the legs/arms (intermittent claudication due to occlusive artery disease). Pentoxifylline can decrease the muscle aching/pain/cramps during exercise, including walking, that occurs with intermittent claudication. Pentoxifylline belongs to a class of drugs known as hemorheological agents. It works by helping blood flow more easily through narrowed arteries. This increases the amount of oxygen that can be delivered by the blood when the muscles need more (such as during exercise) thereby increasing walking distance and duration.

Classification of Drug delivery system

- Controlled release
- Delayed release
- Extended release
- Sustained release
- Site specific targeting

- Receptor targeting

1.1.1 Extended Release Drug Therapy

The term "controlled/extended release" refers to a device that administers medication continuously for a specified duration, exhibiting predictable and consistent kinetics together with a defined release mechanism. This signifies that the medication is dispensed from a controlled release drug delivery system at a kinetically predictable and consistent rate from one unit to another. The system seeks to control the concentration of drug within the target tissue. The flexibility of dosage form design has heightened interest in oral administration for delayed release systems. Multiple interrelated aspects of considerable importance affect the design of oral extended-release delivery systems, including the kind of delivery method and the ailment being addressed.

1.1.2 Matrix Tablet

Matrix tablets are solid oral dosage forms in which the medicine is embedded within a polymer or other excipients' matrix to regulate its release. These systems are engineered to facilitate sustained or regulated drug release, which is especially advantageous for chronic illnesses necessitating long-term therapy.

.Material and Methods

Apparatus and chemicals: Pentoxifylline by Reine Life Science, Gujarat, Microcrystalline Cellulose by Ankit pulps chemicals pvt, Maharashtra, Lactose and magnesium stearate by Zytex biotech pvt limited, Gujarat.

Methods: Preparation of matrix tablet of Pentoxifylline

Compression was carried out in 8 stationed compression machine with 15/7 inch, standard concave plain on both sides. Blended material was loaded in a hopper and powder was compressed to tablets by operating rotary tablet compression machine. Physical parameters like Weight variation, Hardness, Thickness, are monitored to meet the predefined specifications and noted.

Table 1: Formulation for Matrix Tablet formulation

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
Pentoxifylline	400	400	400	400	400	400	400	400	400
Microcrystalline cellulose	60	60	60	60	60	60	60	60	60
Lactose	92.8	92.8	92.8	92.8	92.8	92.8	92.8	92.8	92.8
Povidone k-30	22	22	22	22	22	22	22	22	22
Croscarmellose sodium	18	18	18	18	18	18	18	18	18
Colloidal silicon dioxde	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Magnesium stearate	6	6	6	6	6	6	6	6	6
Total	**600**	**600**	**600**	**600**	**600**	**600**	**600**	**600**	**600**
Coating									
Inner layer									
HPMC K4M (mg)	12	18	6	18	24	12	24	36	12
Isopropyl alcohol	15	22.5	7.5	22.5	30	15	30	45	15
Methylene dichloride	15	22.5	7.5	22.5	30	15	30	45	15
Outer layer									

Hydroxyethyl cellulose (mg)	12	6	18	18	12	24	24	12	36
Isopropyl alcohol	15	7.5	22.5	22.5	15	30	30	15	45
Methylene dichloride	15	7.5	22.5	22.4	15	30	30	15	45
Weight gain (%)	4%	4%	4%	6%	6%	6%	8%	8%	8%
Total weight (mg)	**624**	**624**	**624**	**636**	**636**	**636**	**648**	**648**	**648**

Experimental work

Studies Before Formulation

Preformulation is the study of a medicinal ingredient's physical and chemical qualities, both by itself and when mixed with other ingredients. The goal of preformulation research is to find the physicochemical features and excipients that might have an impact on the final product's manufacturing process, formulation design, and pharmacokinetic-biopharmaceutical aspects.

3.2 Finding out how soluble it is

We examined solubility in several liquids, such as ethanol, methanol, absolute ethanol, acetone, chloroform, ether, water, 10% v/v HCl, and 10% w/v sodium hydroxide.

UV and FTIR Spectroscopy

We next scanned the solution with 10µg/ml at 274 nm to find the wavelength of maximum absorbance. There was a comparison between the reference standard FT-IR spectra of Pentoxifylline and the FT-IR spectrum of Pentoxifylline that was obtained.

Result and discussion

Preformulation Study

4.1.1 Description

Pentoxifylline is white crystalline powder with bitter taste

4.1.2 Result of Solubility

Pentoxifylline dissolves well in water and ethanol, but not so well in toluene.

4.2 Result of Melting Point

The melting point of the medicine was found to be close to the figure given, which confirmed that the drug samples that were received satisfied the requirements. The melting point of a certain drug component will change based on any contaminants that may be there. It is said that pentoxifylline melts around 105°C.

4.3 UV Spectroscopy

A peak with an absorbance was seen at 274 nm in a solution of 10µg/ml in methanol. The identity of the Pentoxifylline molecule is confirmed by the absorbance maxima at 274 nm, which is one of its hallmarks.

4.3.1 FT-IR Spectroscopy

The drug's infrared spectra was similar to that of Pentoxifylline's usual spectrum, which meant that the sample was clean. This confirms that the identification of Pentoxifylline is correct.

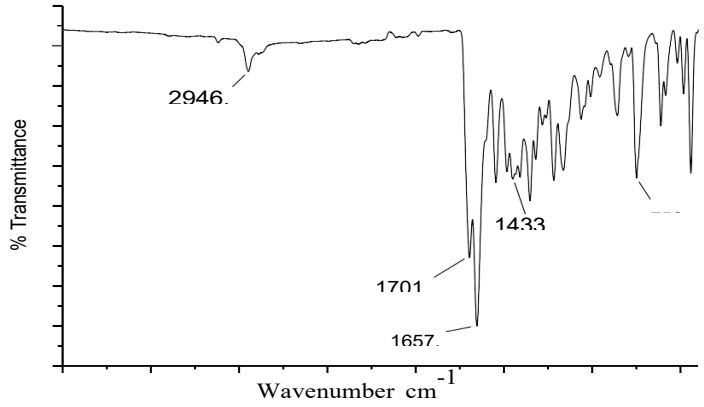

Fig 3. FT-IR of Pentoxifylline

4.4 Drug - Excipients Compatibility Study

FT-IR Spectroscopy

FTIR examination of the physical mixes of the drug and excipients showed that the drug and excipients were compatible.

When you look at the IR spectra of Pentoxifylline, excipients, and their combination, you can see that all of the unique bands in Pentoxifylline are still there.

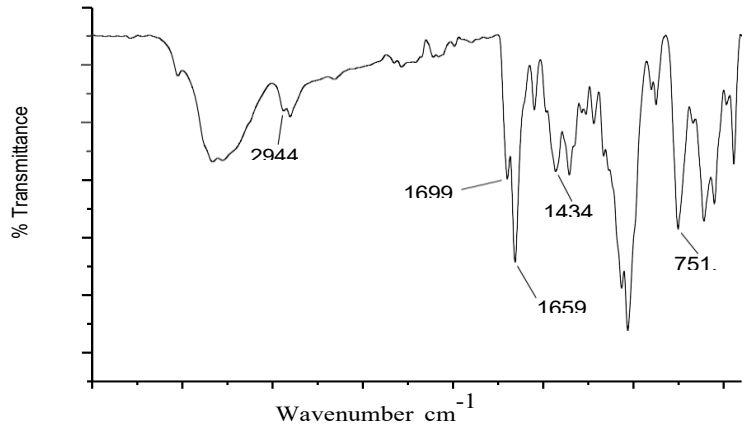

Figure 3 FT-IR Spectra of Pentoxifylline and Excipients

4.5 Evaluation of Matrix Tablet

4.5.1 Pre compression parameters

Table.No.:2. Evaluation parameters of powder blend.

Formulation	Bulk density (g/ml) ± SD	Tapped density (g/ml) ± SD	Carr's index	Hausner's Ratio	Angle of repose(θ)
F1	0.420±0.13	0.478±0.12	12.32±0.49	1.10±0.01	24.39±0.18
F2	0.418±0.11	0.478±0.24	13.14±0.47	1.10±0.14	24.89±0.36
F3	0.425±0.14	0.487±0.11	13.56±0.13	1.26±0.02	25.60±0.28
F4	0.422±0.12	0.480±0.22	13.24±0.20	1.08±0.03	26.10±0.22
F5	0.426±0.11	0.488±0.18	13.46±0.10	1.14±0.04	27.40±0.16

F6	0.422±0.22	0.488±0.15	12.46±0.22	1.18±0.03	24.87±0.44
F7	0.427±0.22	0.482±0.26	12.80±0.30	1.16±0.05	26.90±0.59
F8	0.428±0.17	0.474±0.14	13.44±0.30	1.21±0.05	28.28±0.46
F9	0.424±0.23	0.478±0.17	12.98±0.56	1.18±0.06	24.98±0.41

Table.No.:3. Physical Parameters of Pentoxifylline Matrix Tablets

Formulation	Weight variation**	Thickness*	Hardness (kg/cm2)	Friability (%)	Drug content*
F1	602±0.32	5.3±0.05	7.2±0.06	0.12	99.31±0.17
F2	599±0.28	5.2±0.03	6.8±0.04	0.17	98.64±0.15
F3	600±0.32	5.2±0.02	7.0±0.07	0.17	98.86±0.13
F4	597±0.14	5.1±0.02	7.2±0.04	0.12	99.78±0.16
F5	605±0.26	5.4±0.05	6.8±0.07	0.21	98.80±0.06
F6	603±0.22	5.3±0.02	7.2±0.04	0.12	99.79±0.04
F7	600±0.16	5.2±0.03	7.0±0.03	0.10	98.83±0.13
F8	600±0.14	5.2±0.03	7.2±0.01	0.13	99.45±0.08
F9	598±0.21	5.1±0.02	7.0±0.05	0.12	99.87±0.12

4.5.7 In-vitro release of study

The dissolution release profile of different formulations was examined in vitro. The formulations F1 through F9 were shown to dissolve in vitro based on the findings of controlled release tests. Formulation F8, which has a 12-hour release profile, was chosen to formulate the matrix tablet.

Table.No.:5. In vitro Dissolution profile Pentoxifylline Matrix Tablet release tablets

Time in Hours	%drug release								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0
1	33.32	32.46	38.6	26.42	25.92	28.09	19.42	16.86	20.16
4	77.85	75.68	79.24	56.65	55.12	57.48	36.93	35.62	37.46
8	99.76	99.56	99.97	85.48	84.85	88.66	76.29	73.82	77.37
12	-	-	-	-	-	-	96.56	94.75	97.69

4.6 Release kinetics:

Table 28 : Kinetic studies of matrix Tablets

% drug release	Time t	Square root of time	Log% release	Log t	Log% remain
16.86	1	1.0000	1.2269	0.0000	83.1400

35.62	4	2.0000	1.5517	0.6021	64.3800
73.82	8	2.8284	1.8684	0.9031	26.1400
94.75	12	3.4641	1.9766	1.0792	5.2500

4.7 Stability Studies of best Formulation

Table.No.:6. Stability studies of optimized formulation F8

Parameters	Initial	1st Month	2nd Month	3rd Month
Description	White colour, Caplet shape, Polymer coated tablet.	Complies	Complies	Complies
Average weight (mg)	648	648	647.5	647.3
Thickness (mm)	5.65	5.65	5.64	5.64
Hardness (kg/cm2)	7.2	7.2	7.1	7.1
Assay (%)	99.45	99.45	99.27	99.14
Dissolution	94.75	94.67	94.52	94.43

Conclusion

The 400 mg pentoxifylline multi-layered tablets are created with a wet granulation method that helps them release their contents in a way that doesn't depend on time. The tablet core has a barrier layer on top of it that is both hydrophilic and hydrophobic. This makes the tablet gain 4, 6, and 8% of its weight. Three batches with different polymer ratios were prepared for each proposed weight gain, for a total of nine batches (3X3). It is apparent that making the cover area of the core tablet bigger slows down the pace of breakdown, keeps fluids from touching the core surface, and allows for controlled release.

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