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Formulation and Evaluation of Bilayer of Omeprazole Sustained release action

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ABSTRACT

The purpose of present study is to formulate the bilayer tablets containing omeprazole and diclofenac sodium. In this single tablet omeprazole is in immediate release portion and diclofenac sodium is in sustained released portion. This combination of medicine can be used in the person who are at the threat of developing stomach ulcers. Omeprazole act to relieve ulcers and diclofenac manage to relieve pain due to ulcer. Hence, the layered tablets offer a pharmacokinetic advantage over conventional controlled release lozenge forms as the medicine is snappily released from the fast release subcaste leading to rapid-fire rise of medicine tube attention followed by durability of medicine release from the sustained release subcaste. The optimized immediate release subcaste is named from batches OIR9 grounded on medicine release, wetting down time, and decomposition time. The sustained release tablets are optimized using factorial design for dragged medicine release of diclofenac sodium. Floating bioadhesive tablets are prepared using guar goo and xanthan goo as DSR9 expression. The final bilayer tablet expression (BODT1 – BODT9) is prepared using optimized batches from different polymer combinations. The bilayer tablets parade a unique combination of floatation and bioadhesion for prolonged hearthstone in the stomach and quick onset of action. The polymer- to- medicine rate significantly affects floating pause time and medicine release kinetics. Guar goo and xanthan goo also impact swelling indicator, gastric mucosa adhesion, gastric retention, and in- vitro medicine release rate profile. The optimized expression BODT9 is best suited for GRDDS.

Keywords: Bilayer Tablets, Diclofenac sodium, Omeprazole, Drug, Immediate release, Sustained released, Combination, Drug release, Drug release, Tablets

INTRODUCTION

Sustained Release Drug Delivery

The oral controlled release phrasings have several advantages over a conventional system viz. increased patient compliance, reduced dosing frequence, differencing pharmacological exertion and reduced side goods(Allen 2000, Amir 2000). These systems show significant remedial effect. The CR system gives prolonged delivery of active halves at active point or maintains tube medicine situations in remedial range. In addition, by comparing rate of medicine administration with rate of medicine elimination, a steady state medicine situations in tube can be achieved. The utmost of SR systems shows 1st order kinetics where medicine position in tube is further after administration and diminishes exponentially. Easily depicts tube medicines situations upon administrations of IR and CR phrasings.

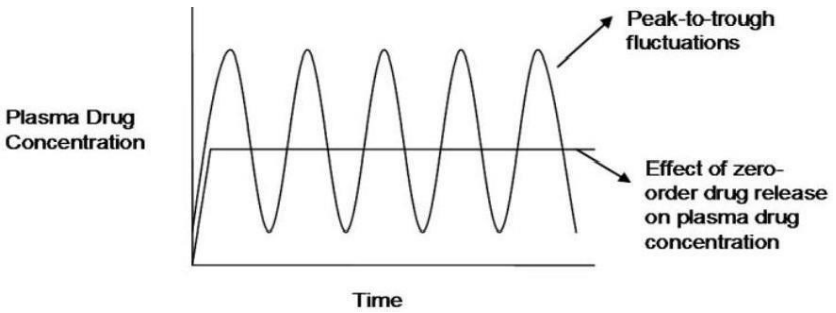


Figure 1.3: Plasma drug level versus time course of conventional and sustained or controlled release formulations

Sustained Medicine release impeccably shows zero order medicine release with extended time of medicine release generally lesser than 12 hours. Several studies are carried out for development of DDS easy to give zero or near zero order release kinetics. From numerous times, the geometric principles have been considered to change medicine release pattern from a non-direct manner to zero or near zero order. The experimenters have tried

to control medicine release way of DDS by altering the figure of medicine delivery bias by using optimization ways e.g., shapes like spherical, globular, a drilled cylinder andbi-convex

The need of changing the figure of bias is to give a constant and stable face area to get zero order release kinetics. Pharmaceutical polymers are pivotal in development of multilayered matrix bias and their characters are also important factors for performance of the bias.

Multi-layered Tablets

Multilayered systems like (bi-layered and tri concentrated tablets etc.) are turns into as a major class of CR bias. These are profitable over conventional tablet systems. Multi layered tablets generally contain, a core subcaste which is girdled polymeric hedge layers composed up of swellable hydrophilic polymers e.g. hydroxyl propyl methyl cellulose and polyethylene oxide and/ or hydrophobic polymers e.g. EC and stearic acid. The hedge layers reduce commerce of active core with GI contents or by reducing the face of device for medicine release and with control of solvent penetration rate and original burst release of the medicine. As time goes, the blown hedge subcaste (s) suffer corrosion and increase in the face area allows medicine to release considerably. generally, a constant medicine release profile can be achieved when both of the hedge layers are hydrophilic in nature and core medicine subcaste should be hydrophobic, the fresh factors also taken into account to get zero order release patterns. Different models oftri-layer tablets and their composition.

Factors influencing Drug Release from Multi-layered Tablets

The multilayered system originally swells, as gel and sluggishly erodes. The effect of polymers on release of venlafaxine HCl. The mix of hydrophilic & swellable polymers like HPMC K100M and Polyol in hedge subcaste and cellulose acetate propionate (hydrophobic) was used in core subcaste that contain venlafaxine HCl. Bi- concentrated and trilayered tablets were prepared by covering one side of core subcaste in case of bi concentrated and two sides were covered to preparetri-layered tablets.

Selection of polymers in designing a controlled release formulation

- Polymers are principally natural or synthetic, high molecular weight macromolecules composed of repeating monomer units linked by covalent chemical bond(Lerk 1979; Liao 2007).
- Bracket of Polymers Polymers are protean in nature and many characters can be adjustable by using some chemical approaches(Longxiao 2000). So, polymers can be classified in numerous aspects like source or characteristics. They can be classified as following
- Natural polymers proteins- collagen, keratin, albumin etc. carbohydrates- bounce, cellulose etc.
- Replicas polymers poly ethylene oxide, poly- esters, poly- amides etc. On base ofbio-response towards polymer
- Non-biodegradable hydrophobic polymers polyvinylchloride, polyethylene
- vinyl acetate
- Biodegradable polymers polyglycolide, polylacticacid, polycaprolactone.
- Addition polymers alkene polymer
- Condensation polymers polyester, polyamides etc. Grounded on heating
- Thermo plastic- polyethylene, polypropylene, Teflon etc.
- Thermo sets- phenolic, urea resin etc.

Materials And Methods

Omeprazole, MCC (Avicel pH 102), SSG, SLS, Lactose anhydrous, Purified Talc, Magnesium stearate

Preparation of Immediate Release Tablets of OMP:

Omeprazole (OMP), Microcrystalline cellulose (MCC 102) was mixed duly with disintegrant (Sodium bounce glycolate (SSG)/ Sodium lauryl sulphate (SLS)) in a mortar according to compositions given in Table 4.1 for 15 min in a demitasse mortar and passed through a# 60 sieve. The mix was mixed with colloidal silicon dioxide and magnesium stearate for 5 min and reused for direct contraction by using a 9 mm round flatfaced punch rotary tablet machine Compression force was kept constant for phrasings. Batch OIR1 to OIR9 are select on the bases on 32 full factorial design and composition of this factorial batches.

Ingredients (mg / tablet)	**Formulations**									
	VP1	**VP2**	**VP3**	**VP4**	**VP5**	**VP6**	**VP7**	**VP8**	**VP9**	**VP10**
Verapamil Hydrochloride	**120**	**120**	**120**	**120**	**120**	**120**	**120**	**120**	**120**	**120**

HPMCK$_{15}$M	**60**	**60**	**60**	**60**	**60**	**60**	**60**	**60**	**60**	**60**
Mannitol	**10**	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**
Micro Crystalline Cellulose	**156.5**	**146.5**	**136.5**	**126.5**	**116.5**	**106.5**	**96.5**	**86.5**	**76.5**	**66.5**
Talc	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**
Magnesium stearate	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**	**1.75**
Total weight (mg)	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**

Table: Compositions of Various Verapamil Hydrochloride Osmotic Controlled Release Matrix Tablets with varying Mannitol Concentration

EVALUATION OF PRE COMPRESSION PARAMETERS

- **Organoleptic Identification**:
  The drug samples were physically linked i.e. Color, odor and taste etc.
- **Bulk & Tapped Density:**
  The medicine greasepaint was exactly counted (M) and poured gently through a glass channel into graduated cylinder and the volume was noted and bulk viscosity was determined. The tapped viscosity was determined using tapped viscosity outfit. A bulk and tapped viscosity of diclofenac sodium is to be 0.309 gm/ ml to 0.311 gm/ ml, and for Omeprazole is to be 0.319 gm/ ml to 0.323 gm/ ml similarly.
- **Partical size**
  The average flyspeck size (davg) of medicine samples were observed by using a phase discrepancy microscope (66172/ Olympus, 100 X, Olympus (India) Pvt. Ltd., New Delhi) fitted with optical micrometer and stage micrometer. The flyspeck size of unmilled diclofenac sodium is to be 33 µm, and for unmilled Omeprazole greasepaint was 51 µm.
- **Flow Properties**
  The inflow parcels of medicine maquillages were characterized in terms of carr's indicator, hausner's rate and angle of repose. The Carr's indicator (IC)) and Hausner's rate (HR) of medicine maquillages were calculating according to following equation
  Carr's Index (IC) = ρTapped - ρBulk / ρTapped
  Hausner's ratio (HR) = ρTapped / ρBulk
  Angle of repose (θ) = $\tan^{-1}$ 2 H / D
- **Solubility determination:**
  The solubility of both medicines API (Omeprazole) was determined in colorful detergents (Water, 0.1 N HCl, phosphate buffer pH 4.5, phosphate buffer 6.8 and phosphate buffer 7.4). Sodium thiosulphate was added to the medium, when phosphate buffer pH 6.8 and phosphate buffer pH 7.4 were used to avoid oxidation. The fat volume of medicine (Omeprazole) was further to 100 ml of medium and stirred constantly overnight at 37 ± 0.5 ºC. The samples were filtered by using Whatman sludge paper (0.45 µm severance size). The solubility assessment of medicine (omeprazole) in 274 nm and 317 nm in different medium was determined spectrophotometrically.

EVALUATION OF POST COMPRESSION PARAMETERS

- **Tablet thikness testing**: The consistence of the tablets (periphery & height) was determined using screw reek.
- **Uniformity of weight of tablet:** Uniformity of weight were determined by tried 20 tablets from each batch and directly counted using an logical balance and average weights were calculated for determination of weight variation.
- **Hardness determination of tablet:** The hardness of tablets is indicates the tensile strength of a tablet. It's expressed in terms of cargo/ pressure needed to crush it when placed on its edge. The tablet hardness was estimated using the Stoke- Monsanto hardness tester. The tablet hardness is expressed in kg.
- **Friability of tablets:** Tablet frangibility test was performed with an average weight of 0.65 g or lower take a sample of whole tablets corresponding to about 6.5 g(20 tablet) at 25 rpm for 4 min using Roches frangibility tester(Model 9509/ ZEC- Z). The chance of frangibility was calculated grounded on the weight lost after the test. A maximum loss of weight(from a single test or from the mean of the three tests) was n't lesser than 1.0.

- **Disintegration test of tablets** The decomposition test was performed using decomposition test outfit(9508/ TEC- 1) Indian Equipment Corp. following the system specified in I.P. etc. using 900 ml of 0.1 N hydrochloric acid.
- **Wetting Study:** doubly folded towel paper was placed in a petri dish having an internal periphery of 5 cm containing 6 ml of water. A immediate release tablets(OIR1- OIR9) was precisely placed on the face of the towel paper in the petri dish. The time needed for water to reach the upper face of the tablet and to fully wet was noted as the wetting time.
- **Swelling Study:** A tablet was counted(W1) and placed in a glass teacup, containing 200 ml of 0.1 N HCl(i.e. pH 1.2), maintained in a water bath at 37 ± 0.5 oC. At regular time intervals, the tablet was taken out and the redundant face liquid was precisely removed by a sludge paper. The study was continued for 8 hrs. The blown tablet was also revisited(W2). The percent lump of sustained release subcaste(DSR1- DSR9) were calculated using the formula. % Swelling = {(W2-W1)/W1)} x 100
- **Determination of drug content**: Tablets were finely pulverized, and a volume of greasepaint fellow to 50 mg of OMP(OIR1 to OIR9) was directly counted. The counted sample transferred to 100 ml volumetric steins containing roughly 50 ml of 0.1 N HCl result. The steins were shaken for solubilizing the medicine and sonicated for 10 min. The volume was adulterated made up to 100 ml by 0.1 N HCl and mixed completely. The medicine samples were adulterated with same detergent up to 10 µg/ ml. The results were filtered through a 0.45 µm membrane sludge and anatomized for the content at 317 nm for OMP independently using double ray UV spectrophotometer(Shimadzu- 1800).
- **In-vitro drug release study:** IP paddle outfit has been used to study in- vitro medicine release from uncoated tablet. In present study, medicine release was studied using a modified IP dissolution rate test outfit(outfit type II) at 100 rpm in 0.1 N HCl as dissolution fluid(900 ml) maintained at 37 ± 0.5 ºC. introverted samples(1 ml) were filtered, anatomized UV spectrophotometrically at at 317 nm for OMP independently. The volume was replaced with the same quantum of fresh dissolution fluid each time to maintain the Gomorrah condition.

Result and Discussion

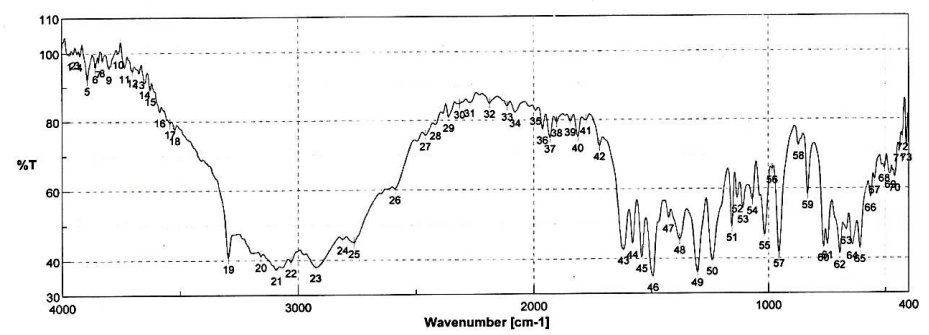
Flow Properties

Table: Flow properties of drug (n = 3)

Drug	Type of powder	Carr's index (%)	Hausner's ratio	Angle of repose θ
Omeprazole	Unmilled	13.08±0.012	1.12±0.021	26.4±0.111
	Milled	10.06±0.016	1.07±0.007	19.2±0.092

IR

Spectrum



Accumulation	35	Resolution	4 cm-1
Zero Filling	ON	Apodization	Cosine
Gain	Auto (126)	Scanning Speed	Auto (2 mm/sec)
Date/Time	3/13/2009 7:40PM	Update	3/13/2009 8:40PM
Operator			
File Name	0309-0706-PT-TRIAZOLE		
Sample Name			
Comment			

No.	cm-1	%T	No.	cm-1	%T	No.	cm-1	%T	No.	cm-1	%T	No.	cm-1	%T
1	3967.82	99.4422	2	3952.39	99.7642	3	3936.97	99.8033	4	3925.39	99.2355	5	3894.54	92.2244
6	3859.83	95.6923	7	3846.33	97.208	8	3829.94	97.5175	9	3801.97	95.4911	10	3762.44	99.9065
11	3736.4	95.6896	12	3702.66	94.4686	13	3674.69	93.9618	14	3650.59	91.0994	15	3626.48	89.1166
16	3585.98	82.7795	17	3542.59	79.4588	18	3523.31	77.6108	19	3294.79	40.8135	20	3156.9	41.2772
21	3091.33	37.3478	22	3030.59	39.5593	23	2925.48	38.0491	24	2810.74	46.0147	25	2761.56	44.9555
26	2588.97	60.34	27	2459.76	75.6917	28	2416.37	78.6969	29	2360.44	80.9224	30	2314.16	84.7794
31	2269.81	85.207	32	2185.92	84.9798	33	2111.67	84.102	34	2077.92	82.2569	35	1992.11	82.7972
36	1963.18	77.2793	37	1932.32	74.799	38	1903.4	79.3505	39	1846.51	79.5382	40	1814.69	74.9858
41	1779.97	79.9308	42	1722.12	72.5153	43	1619.91	42.6677	44	1581.34	44.3134	45	1541.81	40.4064
46	1494.56	34.9265	47	1428.03	51.758	48	1380.78	45.6168	49	1305.57	36.3142	50	1242.9	39.5382
51	1157.08	49.1504	52	1133.94	57.314	53	1109.83	54.353	54	1069.33	56.8065	55	1016.3	46.8039
56	983.518	65.6245	57	954.591	41.6915	58	870.703	72.4935	59	832.133	58.3759	60	764.637	43.2525

Figure : Infrared spectrum of drug sample (Omeprazole)

Tablet Thickness

Formulation code	Tablet Thickness (cm)	
	Thickness	Diameter
OIR1	0.241±0.001	0.81±0.019
OIR2	0.241±0.002	0.80±0.011
OIR3	0.240±0.003	0.81±0.012
OIR4	0.240±0.001	0.81±0.001
OIR5	0.240±0.001	0.80±0.002
OIR6	0.241±0.001	0.80±0.004
OIR7	0.240±0.003	0.80±0.009
OIR8	0.241±0.003	0.80±0.004
OIR9	0.240±0.003	0.80±0.012

Table : Tablet thickness of immediate release layer

Uniformity of weight

Table: Uniformity of weight of immediate release layer

Formulation code	Average Weight (mg)
OIR1	204.2±0.091
OIR2	198.4±0.011
OIR3	203.2±0.058
OIR4	201.8±0.021
OIR5	208.9±0.018
OIR6	197.1±0.001

Hardness

Table : Hardness determination of immediate release layer

Formulation code	Hardness (kg)
OIR1	3.2±0.39
OIR2	3.8±0.29
OIR3	3.5±0.05

OIR4	**3.3±0.13**
OIR5	**3.3±0.22**
OIR6	**3.8±0.23**

- **Friability**

Table: Friability determination of immediate release layer

Formulation code	Friability (%)
OIR1	**0.381±0.61**
OIR2	**0.431±0.11**
OIR3	**0.424±0.32**
OIR4	**0.435±0.14**
OIR5	**0.425±0.44**
OIR6	**0.324±0.24**

Disintegration

Table: Disintegration time determination of immediate release layer

Formulation code	Disintegration time (sec.)
OIR1	**41±1.7**
OIR2	**47±2.1**
OIR3	**59±1.1**
OIR4	**43±1.7**
OIR5	**55±2.8**
OIR6	**51±1.1**

Drug Content

Table: Drug content determination of immediate release layer

Formulation code	Drug content (mg)
OIR1	**49.03±0.72**
OIR2	**49.86±1.09**
OIR3	**49.09±0.01**
OIR4	**49.11±1.11**
OIR5	**49.91±0.32**
OIR6	**49.16±1.19**

CONCLUSION

Point specific or targeting medicine to the stomach is set up to be a new approach during last decade. One of the approaches to develop gastro forgetful medicine delivery system which is designed to aim increased gastric hearthstone time of the lozenge form. Among colorful ways to increase gastric hearthstone time; floating bioadhesive is one of them. expression of immediate release subcaste with bioadhesive sustained release subcaste to develop as a bilayer tablet is the new purpose of this disquisition. With the end bilayer tablet is prepared for giving immediate release of omeprazole to attain onset of action snappily i.e. attaining remedial position with many nanoseconds i.e. maintaining remedial position of medicine for asked time period which is over to 12 hrs. Immediate release tablets of omeprazole were originally prepared by using sodium bounce glycolate and sodium lauryl sulphate as a superdisintegrant, microcrystalline cellulose as a diluent. Superdisintegrant promotes the decomposition and eventually dissolution of medicine; accordingly release rate of medicine increases and its immersion led to briskly onset of action. Optimized immediate release subcaste named from batches OIR9 on the base of medicine release, wetting down time & decomposition time. OIR9 was named as optimized immediate subcaste for the expression bilayer tablet. latterly sustained release tablets were optimized on the base of factorial design for dragged medicine release of diclofenac sodium. In this study floating bioadhesive tablets were prepared using guar goo and xanthan goo as DSR9 expression.

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