Formulation and evaluation of the combined domperidone-pantoprazole delayed-release tablets

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ABSTRACT

The objective of this research was to create and assess a pantoprazole and domperidone combination tablet to lessen patients' pill burden. Both wet granulation and direct compression were used to make pantoprazole sodium core tablets. The powder blends were evaluated for Hausner's ratio, bulk density, tapped density, and angle of repose. The weight fluctuation, hardness, friability, disintegration, and dissolution of compressed tablets were assessed. Batch B3 was chosen for seal coating and enteric coating because it performed better than the other batches. The best enteric-coated batch, PS-EC-03, was chosen after a number of coating parameters were improved, including spray rate (8–19 g/min), inlet air temperature (20–50°C), atomizing air pressure (1–3 bar), and pan rotation speed (5–20 rpm). Domperidone coating was then applied with comparable parameter tuning. Subsequently, Domperidone coating was applied using similar parameter optimization, and one batch was chosen based on assay and accelerated stability results. Pre-compression studies confirmed good flow properties, and compatibility analysis indicated no interactions between the API and excipients. Among the Domperidone-coated formulations, batch F-03 demonstrated the fastest disintegration, highest dissolution and most efficient drug release profile. The study concludes that direct compression followed by optimized coating successfully produced a stable fixed-dose combination tablet, though further work is needed to eliminate yellow spotting in wet-granulated cores.

Keywords: Domperidone; pantoprazole; fixed-dose combination; delayed-release

1. INTRODUCTION

A multicomponent therapy that combines two or more medications is known as a combination therapy. Combination treatment was created with several goals in mind, such as (i) reducing the dosages of drugs with nonoverlapping toxicity. (ii) combining drugs with low cross-resistance to lessen the rate at which acquired resistance emerges. (iii) boosting potency by utilizing additivity, or even better, greater-than-additive effects, in the biochemical activities of two drugs (iv) reducing toxicity (v) using another chemical to make cells more sensitive to a drug's action [1].

In the case of an antihypertensive drug, the purposeful co-administration of two or more well-chosen antihypertensive medications is the foundation of rational combination therapy. The basic prerequisite for every combined antihypertensive drug is that any combination lowers blood pressure more than monotherapy with its component parts. Combining medications from complementary classes generally lowers blood pressure around five times more effectively than raising the dosage of a single medication [2]. Nonetheless, combination therapy has been shown to be required for many chronic infectious diseases and provides a number of benefits over single-drug therapy. In comparison to single-drug therapy, combining drugs may produce additive or synergistic antiviral effects. For instance, seroconversion of hepatitis B surface antigen (HBsAg) or hepatitis B e antigen (HBeAg) may be accelerated by achieving an undetectable HBV DNA level more quickly [3-7].

Dosage formulations with delayed release are the medication is released later after delivery in a sustained release or prolonged action-controlled release dose form. The delayed action is achieved by using a certain kind of coat, such as enteric coating, or other temporal barriers, such as formaldehyde treatment of soft and hard gelatin capsules [8, 9]. There are two variations of delayed release dose forms: time-controlled and site-specific. Drug release from site-specific systems is influenced by two factors: pH and/or the presence of enzymes that trigger drug release. Nevertheless, the system itself influences the release of medication from

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a time-controlled device, such as an osmotic pump with one or more units [10-13]. The purpose of the delayed-release dosage forms is to release the medication only at a certain site in the gastrointestinal tract. The drugs in such a system are: a) known to cause stomach irritation; b) broken down by the stomach or intestinal enzymes; c) meant to have a local effect at a specific GI location; and d) taken from a specific intestinal site [14]. Some advantages are associated with the delayed release dosage form. Such as a) Decrement in drug plasma level fluctuations and maintenance of a constant drug plasma level over an extended period of time, preferably mimicking an intravenous drug infusion, b) Tolerability is increased and negative side effects are decreased by keeping drug plasma levels within a small range without any sudden peaks, c) Reduce the frequency of doses to improve patient comfort and compliance with oral drug delivery system, d) With fewer adverse effects, the delayed release medicine's overall therapeutic cost may be on par with or less than that of the immediate release treatment. There would also be a decrease in the overall cost of disease management; and e) Avoid dosage at night: Patients should also refrain from doing so [15, 16].

Domperidone (DOM) is a benzimidazole compound that has antiemetic and gastrokinetic properties. It is a dopamine2-antagonist with a unique chemical makeup. However, it differs from other gastrokinetic medicines due to its chemical and mode of action [17]. DOM, 5-chloro-1-[1-[3-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)propyl][4-piperidinyl]-1,3-dihydro-2H-benzimidazol-2-one is a weak base with a pKa of 7.89 and a molecular weight of 426. It is almost insoluble in water and has a lipid to water ratio (log P) of 3.90 [18–20]. DOM is sold worldwide in a variety of dose forms with different indications in different nations (e.g., oral tablet, oral solution, rectal suppository) [21]. In Canada, DOM 10-mg tablets are licensed for the symptomatic treatment of upper gastrointestinal motility problems associated with diabetic gastroparesis and chronic and subacute gastritis; in Italy, they are used to treat gastroesophageal reflux disease. However, in the UK, DOM is only advised for the treatment of nausea and vomiting [22]. Numerous side effects of DOM have been reported, including headache, diarrhea, somnolence, cardiac problems, prolactin-related side effects, central nervous system (CNS) side effects, and abdominal pain [23, 24].

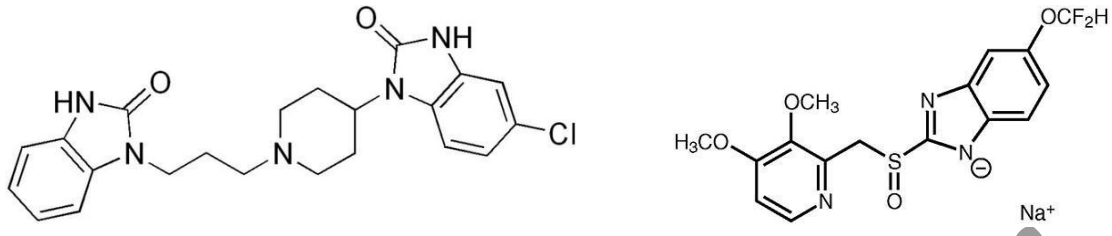
By permanently inhibiting the H+/K+-ATPase enzyme present in the stomach's parietal cells, pantoprazole (PPZ), a membrane-permeable substituted benzimidazole derivative, lowers the generation of gastric acid [25, 26, 27]. Just like other substituted benzimidazole PPIs, PPZ, is a prodrug that is activated and accumulates in an acidic environment and displays tissue selectivity for stomach parietal cells [28,29,30]. Reflux disease and peptic ulcers are treated with PPZ. It is recommended for the management of gastroesophageal reflux disease (GERD)-related erosive esophagitis [31,32]. In short-term (8-week) and a few long-term (up to 4-year) investigations, PPZ has shown high tolerability in individuals with acid-related diseases. However, the most common side effects of PPZ when taken as prescribed were vomiting (2.3%), headache (1.3%), dizziness (0.7%), pruritus (0.5%), nausea (2.7%), and diarrhea (1.5%) [33].

The aim of this work is to develop a combination tablet comprising an enteric-coated core containing Pantoprazole Sodium (PPZS) Sesquihydrate and an immediate-release outer layer of DOM, in order to increase patient compliance and treatment effectiveness for gastroesophageal reflux disease (GERD). Common bi-layer tablets production problems, such as layer separation, resistance to form dense compacts, inadequacy in active coating, weight irregularities, and surface roughness, are intended to be addressed by this dual-layer

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formulation. The distinguishing feature of the present study is the dosage-form architecture: pantoprazole sodium is incorporated into an enteric-coated core, while domperidone is applied as an immediate-release outer coating on the same dosage form.



Domperidone Pantoprazole Sodium

Figure 1. Chemical structure of Domperidone and Pantoprazole Sodium

2. MATERIALS AND METHODS

2.1 Sources and qualities of chemicals and reagents

Zydus Cadila Ltd. gladly offered a free sample of PPZS Sesquihydrate. Mannitol SD-200, Microcrystalline cellulose pH 102, Kollidon CL (cross povidone), low substituted HPC as well as color coatings EC4S and FC4S was supplied by Corel Pharma Chem., Ahmedabad, India. Relasions International Ltd gifted DOM from Maple Biotech Pvt. Ltd., India. Heavy magnesium oxide was obtained from Roquette Frères, France. Methanol and Methylene chloride were supplied by Luzenac Pharma, Italy. Additionally, Opadry Milky White was obtained from Canton Laboratories Ltd., India. All the chemicals and ingredients used were of analytical grade.

2.2 Formulation and evaluation of pantoprazole sodium core tablets

2.2.1 Characterization and estimation of pantoprazole sodium in API

Preformulation is a branch of pharmaceutical science that studies the physical and chemical characteristics of medicinal components both on their own and in combination with excipients to ascertain the physicochemical properties of the drug substance. It is crucial to identify the basic physical and chemical characteristics of the drug product before developing of any novel dosage forms [34-36]. A number of tests were carried out including bulk characterization, solubility analysis, stability analysis, and micromeritic property evaluation to characterize the pharmaceutical ingredients. Bulk characterization indicating the assessment of particle size, shape, density, purity, crystallinity, polymorphism, hygroscopicity, and surface area [37]. A solubility examination of a new drug in a stomach-simulated media is crucial since solubility influences a medication's effectiveness. The methods utilized in solubility analysis include membrane permeability, partition coefficient, pKa measurement, solubility determination, and common ion effect [38]. Micromeritic characteristics were assessed using a variety of metrics, including as Hausner's ratio, compressibility index, bulk and tapped density, and angle of repose [38]. A number of measures, including Hausner's ratio, compressibility index, bulk and tapped density, and angle of repose, were used to evaluate micromeritic properties [39]. High-performance liquid chromatography (HPLC), UV-visible spectrophotometry, and titrimetric methods employing 0.1 N HCL and 6.8 pH phosphate buffer were among the methods used to estimate the PPZS in order to ensure its potency and purity [40].

2.2.2 Drug excipients compatibility study

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Drug-excipient compatibility research is an important step in the development process because potential physical and chemical interactions between the API and the formulation's constituents might affect a drug's chemical nature, stability, bioavailability, therapeutic effectiveness, and safety [41-43]. PPZS was used to carry out drug and excipient compatibility study with different excipients in varied ratios maintaining environmental condition 40°C and 75%RH. The API was combined with magnesium oxide (1:5), calcium carbonate (1:4), and mannitol (1:2). In order to determine the effect on drug stability, the compatibility was also assessed with disintegrants, binders, lubricants, and coating materials like microcrystalline cellulose (MCC pH 102) (1:1), crosspovidone (1:0.5), magnesium stearate (1:0.25), talc (1:0.25), and Color coat FC4S (1:2).

2.2.3 Formulation development and evaluation of core tablet

PPZS core tablets were manufactured through both wet granulation and direct compression methods. Direct compression technique were used for batches B1 to B6, while B7 to B9 were prepared through wet granulation. Wet granulation incorporated low-substituted sodium hydroxide as a stabilizer, mannitol as a diluent, [44] low-substituted hydroxypropyl cellulose (HPC) as a binder, [45] magnesium stearate as a lubricant, [46] and isopropyl alcohol as a solvent. In Direct compression formula different excipients were used with a variety of effects like as sodium hydroxide, calcium carbonate, and magnesium oxide used as stabilizers,[47] while excipients like mannitol, microcrystalline cellulose, and cross povidone improve compressibility and disintegration [48 49]. Powder blends were tested for angle of repose, bulk density, tapped density, Hausner's ratio, and blend homogeneity as well as blend uniformity of 100 mg PPZS powder blend was assessed with pH 6.8 phosphate buffer, filtered with (0.45 µm), and its absorbance measured at 284 nm using a Shimadzu UV-1700 spectrophotometer [50]. Moreover, some physical properties of the formed tablets like hardness, friability, weight variation, and disintegration time were assessed.

2.2.4 Formulation and evaluation of delayed-release enteric coating tablets

The preparation of the coating solutions involved two stages: seal coating and enteric coating. For the seal coating, color coat FC4S (10%) was dissolved in a mixture of Isopropyl Alcohol (40%) and Methylene Dichloride (60%) under constant stirring for 15–20 minutes. This solution was then applied to the core tablets to prevent any interaction between PPZS and the subsequent enteric coating, with a final weight gain of 3%. For the enteric coating, color coat EC4S was dissolved in a solvent mixture of Iso Propyl Alcohol (72-77%) and Methylene Dichloride (28-42%). The appropriate amount of Color coat EC4S (8-15%) was added, and the mixture was agitated for 15-20 minutes to create a homogeneous coating solution. The tablets were coated using a side-ventilated, perforated pan coating machine (Gans coater GAC 275). The tablets from the B3 batch were divided into four groups and placed on a pan warmed to 50°C for 5–10 minutes. The coating solution was then applied under regulated conditions, which included spray rates of 8-25 gm/min, intake air temperatures of 20-50°C, atomizing air pressures of 1-3 bar, and pan rotation speeds ranging from 5 to 20 rpm. After applying the coating, the tablets were cooled at 40°C with a pan speed of 2 rpm to guarantee uniform coating hardening.

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The evaluation of enteric-coated Pantoprazole Sodium tablets included determining coating uniformity (CU), moisture content (% LOD), and optimizing coating parameters such as spray rate, inlet air temperature, atomizing air pressure, and pan rotation speed. Coating homogeneity was assessed by weight gain, and percentage LOD was estimated by drying tablets at 60°C for 24 hours. The uniformity of medication content was determined by UV-visible spectrophotometry at 284 nm after dissolving powdered tablets in phosphate buffer (pH 6.8). Disintegration testing was performed according to USP guidelines in 0.1N HCl (pH 1.2) for 2 hours, then in phosphate buffer (pH 6.8) for 1 hour. In vitro drug release investigations were performed using a USP type II dissolution equipment at 100 rpm in 0.1N HCl for 2 hours and phosphate buffer (pH 6.8) for 1 hour, with absorbance measurements taken at 260 and 284 nm.[51]

2.3 Formulation and evaluation of immediate release coating layer of domperidone over enteric-coated delayed-release tablets of pantoprazole sodium

2.3.1 Preparation of color dispersion

The color dispersion for DOM's immediate-release layer was made by creating a vortex by agitating methanol and Opdry Milky White in a stainless-steel bucket for 5 minutes. Methylene chloride and heavy magnesium oxide were then added, and the mixture was continuously stirred for 15 minutes. Finally, DOM maleate was added to the vortex and mixed for another 30 minutes. The formulation included variable quantities of Opdry Milky White, methanol, methylene chloride, and heavy magnesium oxide over five batches (F1-F5), whereas the amount of DOM stayed constant at 92g.

2.3.2 Coating of tablets

Using a perforated pan coating machine the coating of DOM tablets was carried out. Tablets were warmed at 40°C for 5-10 minutes before weighing. The coating solution was made in five batches (F1–F5), and the coating process was optimized by modifying parameters such as spray rate (3-15 g/min), intake air temperature (20-50°C), atomizing air pressure (1-3 bar), and pan rotation speed (5-20 rpm). After coating, the tablets were dried and cooled in a pan at 40°C and 2 rpm before being removed and tested for various quality parameters. Several coating problems such as sticking, rough surface, nozzle choking, and formation of excessive dust were evaluated for determining the optimal conditions. In-vitro disintegration tests were performed using a Tablet Disintegration Tester in distilled water at 37 ± 2°C. Wetting time was assessed by placing tablets on tissue paper in a dye solution, recording the time for water to reach the tablet's upper surface. A USP Type II dissolution apparatus was used in 0.1 N to conduct in 0.1 N HCl (pH 1.2) at 37 ± 0.5°C and 50 rpm, with samples analyzed via UV spectrophotometry at 284 nm to determine the cumulative release of drug.

2.3.4 Assay of domperidone coating layer

The homogeneity of DOM coating layer's is assessed by using the UV-visible spectroscopy. A phosphate buffer of pH 6.8 was used and the medication was extracted from a sample of coated tablets which had been roughly pulverized. Finally, the content of drug was determined using a calibration curve, and the absorbance was measured at wavelengths that corresponded to

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DOM. The absorbance was measured at certain wavelengths that correlate to DOM, and the drug content was estimated using a calibration curve.

3. RESULTS

3.1 Formulation and evaluation of core tablets of Pantoprazole Sodium

3.1.1 Characterization and estimation of API

The micromeritic characteristics of powder blends and API from various batches of PPZS core tablets were evaluated. The assessment of the micromeritic or physical characteristics of API and powder blends, such as bulk density, tap density, percent compressibility index, and Hausner ratio, is presented in Tables 1 and 4. According to published research, powders with a Hausner ratio of less than 1.25 have adequate flow ability, and those with a percent compressibility index between 5% and 18% are appropriate for making tablets [52].

Table 1: Micromeritic properties of API

Sample	Angle of repose (0)	Bulk density (g/ml)	Tapped density (g/ml)	Compressibility Index (%)	Hausner's ratio
API	31	0.336	0.506	29.36	1.37

3.1.2 Drug excipients compatibility study

Compatibility study of PPZS with different excipients in different ratio was performed by maintaining the environmental condition as temperature (40°C ± 2°C) and % (RH 75% ± 5 %) for four weeks. Table 2 represent the data of Drug Excipients Compatibility Study.

Table 2: Drug Excipients Compatibility Study

Materials	Initial Observation	Drug : excp. ratio	Duration in Weeks				
			0	I	II	III	IV
Pantoprazole Sodium	A white to almost white powder	1:1	Complies	Complies	Complies	Complies	Complies
Drug+$CaCO_3$	A white to almost white powder	1:4	Complies	Complies	Complies	Complies	Complies
Drug+Mg-oxide	A white to almost white powder	1:5	Complies	Complies	Complies	Complies	Complies
Drug + Mannitol	A white to almost white powder	1:2	Complies	Complies	Complies	Complies	Complies
Drug + MCC pH 102	A white to almost	1:1	Complies	Complies	Complies	Complies	Complies

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	white powder						
Drug + Cross povidone	A white to almost white powder	1:0.5	Complies	Complies	Complies	Complies	Complies
Drug+ Mg-stearate	A white to almost white powder	1:0.25	Complies	Complies	Complies	Complies	Complies
Drug + Talc	A white to almost white powder	1:0.25	Complies	Complies	Complies	Complies	Complies
Drug+All excipients	A white to almost white powder	1:1	Complies	Complies	Complies	Complies	Complies

3.1.3 Formulation development and characterization of powder blend

PPZS tablets were prepared by both direct compression and wet granulation method. Batches B1 to B6 were prepared by direct compression method and batches B7 to B9 were prepared by wet granulation method. Table 3 is representing the overall formula from batch B1 to B9.

Table 3. Formulation of different batches of Pantoprazole sodium core tablets

Ingredients	**Direct Compression**						**Wet Granulation**		
	B1	**B2**	**B3**	**B4**	**B5**	**B6**	**B7**	**B8**	**B9**
Pantoprazole Na	20	20	20	20	20	20	20	20	20
Sodium hydroxide	-	-	-	-	-	-	2.0	2.3	2.5
Calcium carbonate	-	-	-	40	50	60	-	-	30
Magnesium oxide	60	70	80	-	-	-	-	30	-
Mannitol	50	60	40	70	80	60	90	60	60
Mcc PH 102	30	10	20	30	10	20	-	-	-
Low HPC	-	-	-	-	-	-	30	30	30
Isopropyl alcohol	-	-	-	-	-	-	q.s	q.s	q.s
Crosspovidone	5	5	5	5	5	5	5	5	5
Magnesium stearate	2	2	2	2	2	2	2	2	2
Total	171	171	171	171	171	171	153	153.3	153.5

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Table 4 : Micromeritic properties of powder blends of different batches

Powder blend	Angle of repose (0)	Bulk density (g/ml)	Tapped density (g/ml)	Hausner's ratio	Compressibility Index (%)	Drug Content (%)
B1	21	0.426	0.515	1.18	16.0	97.44
B2	22	0.432	0.519	1.17	15.0	96.37
B3	19	0.438	0.504	1.19	16.5	99.74
B4	27	0.390	0.521	1.30	23.0	97.56
B5	32	0.389	0.526	1.36	26.0	95.39
B6	29	0.396	0.536	1.35	27.0	98.47

3.1.4 Evaluation of core Tablets

Different physical properties like Appearance, Weight variation, Diameter, Thickness, Hardness, Friability, DT and Dissolution profile of uncoated Tablets of PPZS was evaluated. All the data about physical parameters of uncoated tablets from batch B1 to B9 are depicting the Table 5.

Table 5: Evaluation parameters of Uncoated Tablet of Pantoprazole Sodium

Parameters	Batches								
	B1	B2	B3	B4	B5	B6	B7	B8	B9
Appearance	-	-	-	-	-	-	Yellow spots	Yellow spots	Yellow spots
Weight variation	171± 1.64	171 ±2.43	171± 1.72	171± 2.65	171± 2.54	171± 1.86	153± 2.54	153± 0.69	153± 1.84
Diameter (mm)	8.04	8.04	8.04	8.04	8.04	8.04	8.04	8.04	8.04
Thickness (mm)	2.91	2.93	2.94	2.98	2.97	2.98	2.75	2.76	2.75
Hardness	6.5	5.5	6.5	5.5	6.0	5.0	6.0	6.5	5.5
Friability (%)	0.37	0.52	0.13	0.46	0.33	0.61	0.60	0.43	0.67
Disintegration time (min.)	6.35	5.15	4.50	6.35	5.24	4.53	5.52	6.43	5.36
Dissolution (after 45 min)	92.48 %	94.37 %	98.82 %	89.87 %	95.67 %	94.54 %	83.36%	73.79 %	85.57 %

3.1.5 Assay of Pantoprazole Sodium Uncoated Tablet

Table 6: Assay of Uncoated Tablet of Pantoprazole sodium

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Claim/Tablet Pantoprazole Sodium 20mg	**Specification** 18 mg to 22 mg of Pantoprazole Sodium (90% to110% of the labeled amount of Pantoprazole Sodium)	19.89 mg (99.45%)

3.1.6 Formulation of Seal Coating solution (colorcoat FC4S)

To prevent interaction between PPZS and Colorcoat EC4S, seal coating of core tablets of PPZS was done by Colorcoat FC4S until weight gain 3%. Table 7 is representing the data of composition of seal coating solution and table 8 is also providing the data regarding the formulation of enteric Coating solution.

Table 7. Composition of colorcoat FC4S coating solution

Material	Quantity (%)
Colorcoat FC4S	10.0
Iso Propyl Alcohol	40.0
Methylene Dichloride	60.0

3.1.7 Formulation of Enteric Coating solution of (colorcoat EC4S)

Table 8: Formulation of Colorcoat EC4S coating solution

Material Quantity (%)	PS-EC-01	PS-EC-02	PS-EC-03	PS-EC-04
Colorcoat EC4S	10.0	8	13	14
IsoPropylAlcohol	72.0	66	67	78
Methylene Dichloride	28.0	35	30	42

3.1.8 Optimization of various parameters of coating operation

During coating operation different coating parameter like Spray rate, inlet air temperature, atomizing air pressure, pan rotation speed was optimized and the results are showing in the table 9 to 12 and table 13 is providing the data of evaluation parameters of enteric coated Tablet.

Table 9: Optimization of spray rate

Batch	Spray rate (gm/min)	Problem during coating
PS-EC-01	8	Rough Surface
PS-EC-02	13	-
PS-EC-03	16	-
PS-EC-04	19	Rough Surface

Table 10: Optimization of inlet air temperature

Batch	Inlet air temperature (°C)	Problem during coating

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PS-EC-01	20	Sticking and Picking
PS-EC-02	30	-
PS-EC-03	40	-
PS-EC-04	50	Choking of Nozzle

Table 11: Optimization of atomizing air pressure

Batch	Atomizing air pressure (bar)	Problem during coating
PS-EC-01	1.0	Sticking and Picking
PS-EC-02	1.5	-
PS-EC-03	2.0	-
PS-EC-04	2.5	Excess dust Formation

Table 12: Optimization of Rotating speed of pan

Batch	Rotating speed of pan (rpm)	Problem during coating
PS-EC-01	5	-
PS-EC-02	10	-
PS-EC-03	15	-
PS-EC-04	20	twinning

3.1.9 Evaluation of enteric coated Tablet of Pantoprazole sodium

Table 13: Evaluation parameters of enteric coated Tablet

Parameters	Batches			
	PS-EC-01	PS-EC-02	PS-EC-03	PS-EC-04
Appearance	A almost white color round shallow biconvex tablet	A almost white color round shallow biconvex tablet	A almost white color round shallow biconvex tablet	A almost white color round shallow biconvex tablet
Weight variation	182±2.3	181±1.2	180±1.76	183±3.2
Diameter (mm)	8.89	8.86	8.95	8.97
Thickness (mm)	2.95	2.89	2.87	3.02
Disintegration time (min.)	12.46	11.18	11.04	14.93
Dissolution Rate	89.93%	92%	97.86%	86%

3.2 Formulation and evaluation of immediate release coating layer of Domperidone over enteric coated delayed release tablets of Pantoprazole Sodium.

3.2.1 Domperidone coating was done over the enteric coated Tablet of Pantoprazole sodium. Table 14 representing the preparation formula of color dispersion of domperidone. Different coating parameter like Spray rate, inlet air temperature, atomizing air pressure, pan rotation speed was optimized during coating operation and the results are showing in the table from 15 to 18 and table 19 is providing the data of evaluation parameters of domperidone coated

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Tablet respectively. However, table 20 is depicting the assay result of Domperidone coating layer and table 21 is providing three month's accelerated stability study data.

Table 14: Formulation for domperidone coating solution

Ingredients	Batch Codes				
	F1	F2	F3	F4	F5
Domperidone (gm)	92	92	92	92	92
Opdry Milky white(ml)	300	350	375	400	450
Methanol(ml)	320	340	360	380	400
Methylene Chloride(ml)	200	225	250	275	300
Heavy magnesium oxide(Mg)	75	95	120	135	160

3.2.2 Coating procedure of Tablets with coating parameter optimization

Table 15: Optimization of spray rate

Batch	Spray rate (gm/min)	Problem during coating
F-01	3	Rough Surface
F-02	6	-
F-03	8	-
F-04	10	Rough Surface
F-05	12	Twining of tablets

Table 16: Optimization of inlet air temperature

Batch	Inlet air temperature (°C)	Problem during coating
F-01	15	Sticking and Picking
F-02	20	-
F-03	25	-
F-04	30	Choking of Nozzle
F-05	35	Choking of Nozzle

Table 17: Optimization of atomizing air pressure

Batch	Atomizing air pressure (bar)	Problem during coating
F-01	1.0	Sticking and Picking
F-02	1.5	-
F-03	2.0	-
F-04	2.5	Excess dust Formation
F-05	3.0	Rough Surface

Table 18: Optimization of Rotating speed of pan

Batch	Rotating speed of pan (rpm)	Problem during coating

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F-01	5	-
F-02	10	-
F-03	15	-
F-04	20	sticking
F-05	25	sticking

3.2.3 Evaluation of Domperidone coated Tablet

Table 19: Evaluation parameters of Tablet after Domperidone Coating

Parameters	**Batches**				
	F-01	**F-02**	**F-03**	**F-04**	**F-05**
Appearance	A white color round shallow Biconvex tablet	A white color round shallow Biconvex tablet	A white color round shallow Biconvex tablet	A white color round shallow Biconvex tablet	A white color round shallow Biconvex tablet
Weight variation	205±1.9	207±1.6	208±1.10	207±2.7	209±2.5
Diameter (mm)	9.13	9.22	9.50	9.48	9.66
Thickness (mm)	3.41	3.37	3.43	3.03	3.36
Disintegration time (In Sec.)	33	31	26	29	35
Dissolution Rate	93.26%	95.78%	98.87%	90.46%	95.84%

3.2.4 Assay of Domperidone coating layer

Table 20: Assay of Domperidone coating layer

Claim/Tablet Domperidone 10mg	**Specification** 9 mg to 11 mg of Domperidone (90% to110% of the labeled amount of Domperidone)	9.58 mg (95.87%)

3.2.5 Accelerated stability study of best batch (F-03)

The stability studies were carried out for the optimized F-03 formulation for three months and it showed acceptable results.

Table 21: Comparison of parameters for Batch F-03 Initial and after three months

Parameters	**Batch F-03 (Initial)**	**Batch F-03 (after three months)**
Disintegration time	26 sec	31 sec
Dissolution rate	98.87%	96.44%
Wetting time	28 sec	32 sec

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4. DISCUSSION

The micromeritic profiling of PPZS and its blends constituted the initial essential step in evaluating their suitability for a solid oral formulation. With a bulk density of 0.336 g/ml, tapped density of 0.506 g/ml, and an angle of repose of 31°, the pure API produced a compressibility index of 29.36% and a Hausner ratio of 1.37. The well-known processing difficulties of proton-pump inhibitors are echoed by these data, which show cohesive powder with restricted flow and a strong tendency toward consolidation [53]. Prior to scaling up, a compatibility study conducted over four weeks at 40 ± 2 °C and 75 ± 5% relative humidity verified that the API and its binary blends maintained a white to almost white powder look and satisfied all predetermined requirements, confirming chemical and physical stability [54].

Both wet and dry granulation methods were investigated in order to convert the cohesive powder into a free-flowing, compressible intermediate. Wet granulation (batches B7–B9) used low-substituted hydroxypropyl cellulose (L-HPC) as a multipurpose binder disintegrant, sodium hydroxide to provide an alkaline microenvironment that prevents acid-catalyzed degradation of pantoprazole, and isopropyl alcohol as the processing solvent [55,56]. As substitute alkalizing fillers that could affect dissolving behavior, magnesium oxide in B8 and calcium carbonate in B9 were studied [57]. Batches B1–B6 were, however, made by direct compression in order to test the viability of a quicker, solvent-free procedure. The alkalizing agents in this case were magnesium oxide (B1–B3) or calcium carbonate (B4–B6). Cross-povidone accelerated the disintegration process, and mannitol and microcrystalline cellulose PH102 balanced tablet strength, flow, and compressibility [58]. A consistent amount of magnesium stearate was added as a lubricant [59].

There were notable differences in granule flowability amongst formulations. For B1–B3, the compressibility indices were 15.0–16.5 percent, the Hausner ratios were 1.18–1.19, the bulk densities were 0.426–0.438 g/ml, and the angles of repose were 19°–22°. These values indicate excellent flow and moderate packing behavior [60]. The less compressible character of calcium carbonate-rich blends is supported by the comparison of B4–B6, which showed angles of 27°–32°, lower bulk densities (0.389–0.396 g/ml), and inferior flow indices (Hausner 1.30–1.36; CI 23.0–27.0%) [61]. All batches showed high assay uniformity (95.39–99.74%), with B3 having the highest drug content (99.74%), highlighting sufficient blend homogeneity independent of process technique [62].

Core tablet evaluation confirmed the benefits of the direct-compression magnesium oxide series. B1–B6 did not exhibit the yellow specks as seen in wet-granulated tablets (B7–B9), suggesting that the solvent, moisture, and heat-exposed procedure may cause color changes as a result of oxidative degradation in the heat- and moisture-sensitive API [63]. Wet-granulated products were slightly thinner (~2.75 mm) than their directly compressed equivalents (2.91–2.98 mm), but all tablets met pharmacopoeial limit for weight fluctuation [64]. Batches made with magnesium oxide (B2, B3) produced the most durable compacts without sacrificing disintegration, and tablet hardness ranged from 5.0 to 6.5 $kgcm^{-2}$ [65]. Mechanical resilience was confirmed by the friability readings, which were comfortably below 1%, with B3 at an exceptionally low 0.13 %. While all cores disintegrated quickly (4.50–6.43 min), B3 and B6 disintegrated the quickest, which was consistent with cross-povidone efficiency [66]. After 45 minutes, B3's dissolution rate was 98.8%, followed by B5's at 95.67% and B6's at 94.54%, indicating that B3 offers the best release pattern. Each tablet contained 19.89 mg of PPZS

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(99.45% of the label), according to assay of uncoated cores, exhibiting excellent dosage precision [67].

As pantoprazole is acid-labile, a Color Coat EC4S enteric system (batches PS-EC-01 to PS-EC-04) was used to protect the cores. To optimize film formation, various isopropyl alcohol/methylene chloride ratios were investigated in conjunction with polymer loadings ranging from 8 to 14% w/w [68]. Important process parameters were promptly determined. A rough surface was formed by spray rates below 13 gm/min, while an excessive 19 gm/min encouraged droplet coalescence. In a similar vein, inlet temperatures needed to be balanced: coatings produced at 30 to 40 °C were smooth and continuous, while sticking or picking occurred at 20 °C and nozzle blockage occurred at 50 °C. Dust and twinning were reduced by using pan speeds of 5 to 15 rpm and optimal atomization of 1.5 to 2.0 bar [69]. In contrast to the other enteric variations, PS-EC-03 tablets coated under this intermediate conditions disintegrated in 11.04 minutes and released 97.86% of the medication in 45 minutes.

To ensure synchronized release in the fixed-dose combination, a parallel film-coating procedure was used for the co-administered DOM layer. Opadry milky white (300–450 mL) and heavy magnesium oxide (75–160 mg) were increased to produce consistently white, biconvex tablets (9.13–9.66 mm in diameter), with a progressive improvement in film strength and consistency. Batch F-03 created the most consistent film when the temperature, atomization pressure, spray rate, and pan speed were all moderate. F-03 met regulatory standards with a 98.87 percent dissolution and an assay of 9.58 mg (95.87 percent of label claim). A three-month accelerated study on F-03 at 40 °C and 75% relative humidity confirmed the coating's chemical stability and toughness by showing only minor increases in disintegration time and very little loss of dissolving [70].

Together, the findings show that when combined with magnesium oxide, cross-povidone, and MCC PH102, PPZS can be effectively processed into premium enteric tablets through a direct compression method. The downstream DOM coating stays stable under accelerated conditions, and protection in gastric media is maintained while maintaining rapid release at intestinal pH, thanks to careful enteric-coating parameter optimization. The optimized formulation demonstrated favorable physical characteristics, disintegration, dissolution, assay, and preliminary accelerated-storage performance under the conditions investigated. The formulation architecture was designed to combine rapid domperidone release with delayed pantoprazole release from a single tablet. Further work is required, including formal analytical-method validation, complete pH-shift and final-product sequential dissolution testing, replicate-based statistical evaluation, extended stability studies, and appropriate in vivo or clinical evaluation before broader therapeutic or commercial conclusions can be drawn.

5. CONCLUSION

Combining DOM and PPZS Patients with gastro-oesophageal reflux disease (GERD) may be treated with a tablet that has an immediate-release outer layer of DOM and a delayed-release enteric-coated core tablet of pantoprazole sodium. Following pre-formulation research, it was determined to make PPZS tablets using both wet granulation (B7 to B9) and direct compression (B1 to B6). The granules were assessed for bulk density, tapped density, compressibility index, and Hausner's ratio prior to compression. Weight variation, hardness, friability, disintegration time, and in vitro drug release were assessed for the compressed tablets. On the surface of the tablets manufactured using the wet granulation method, however, yellow spots were visible.

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from nine distinct formulations (B1 to B9) Batch B3 was ultimately chosen for seal coating, followed by enteric coating. Then fixed quantity tablets from B3 batch were selected and divided into 4 batches. From the results of different coating parameters, after finishing enteric coating it was found that PS-EC-03 batch was shown good disintegration time and drug release as compare to other 3 batches (PS-EC-01, PS-EC-02, PS-EC-04). Finally, Batch PS-EC-03 was selected for DOM coating. The coating solution of DOM is formulated in five batches (F1 through F5). Once all batches of tablets have been coated, they are assessed using a number of metrics, including weight gain, disintegration time, in-vitro drug release, spray rate (gm/min), inlet air temperature (°C), atomizing air pressure (bar), and pan rotation speed (rpm). It was found that after DOM Coating F-03 is the best batch. It was then selected for accelerated stability test. The stability studies were carried out for the optimized F-03 formulation for three months and it showed acceptable results. So it was concluded that by with direct compression and coating, it is possible to prepare the tablets of DOM and PPZS in combination by a common compressing method as it satisfied all the criteria and it would be alternative to the currently available conventional single-drug tablets of DOM and Pantoprazole Sodium. The technique adopted was found to be economical and industrially feasible. However, it is to be noted that yet there is still an aspect that can be studied in the future is more analysis on the removal of yellow spots on the surface of tablets produced by powder blend manufactured by wet granulation method as wet granulation technique is more convenient, low dust generating, high yield percentage of granules and more industrially feasible.

CLINICAL TRIAL NUMBER

Not applicable

ETHICAL APPROVAL

Not applicable

CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

AUTHORSHIP CONTRIBUTION

Conceptualization, A.B.S.; methodology, A.B.S.; experimental observation, D.R.S., R.D. and T.R.; software, R.I.,; validation, A.B.S., T.R. D.R.C. and D.R.S.; formal analysis, S.G., M.I.J.O., T.R., S.C.D. and M.M.M.; data curation, R.I., and M.M.M.; funding acquisition, M.M.M.; writing—original draft preparation, M.I.J.O., and A.B.S.; writing—review and editing, M.I.J.O. and A.B.S.; mechanisms drawing, M.I.J.O.; supervision, A.B.S.; project administration, A.B.S.

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REFERENCES

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https://doi.org/10.71193/jmct.20260017
Journal Home Page: Journal of Medicinal Chemistry and Therapeutics

1. Systems biology and combination therapy in the quest for clinical efficacy; Jonathan B Fitzgerald, Birgit Schoeberl, Ulrik B Nielsen & Peter K Sorger; volume 2 number 9 september 2006
2. Wald DS, Law M, Morris JK, et al. Combination therapy versus monotherapy in reducing blood pressure: meta-analysis on 11,000 participants from 42 Trials. Am J Med 2009; 122: 290–300.
3. Pawlotsky JM. Virology of hepatitis B and C viruses and antiviral targets. J Hepatol 2006;44(1 Suppl): S10-S13.
4. Yokota T, Mochizuki S, Konno K, Mori S, Shigeta S, De Clercq E. Inhibitory effects of selected antiviral compounds on human hepatitis B virus DNA synthesis. Antimicrob Agents Chemother 1991; 35: 394-397.
5. Seifer M, Hamatake RK, Colonno RJ, Standring DN. In vitro inhibition of hepadnavirus polymerases by the triphosphates of BMS-200475 and lobucavir. Antimicrob Agents Chemother 1998; 42: 3200-3208.
6. Seigneres B, Pichoud C, Martin P, Furman P, Trepo C, Zoulim F. Inhibitory activity of dioxolane purine analogs on wild-type and lamivudineresistant mutants of hepadnaviruses. HEPATOLOGY 2002; 36: 710-722.
7. Standring DN, Bridges EG, Placidi L, Faraj A, Loi AG, Pierra C, et al. Antiviral beta-L-nucleosides specific for hepatitis B virus infection. Antivir Chem Chemother 2001;12(Suppl 1):119-129.
8. Jantzen GM, Robinson JR. Sustained and controlled release drug delivery system. In BankerGS, Rhodes CT, editors. Modern pharmaceutics. 3rd edition New york: Marcel dekkerInc;1996.p.575-09.
9. Lachman Leon, Lieberman Herbert A. Compression coated and layer tablets. In: Pharmaceutical Dosage Forms: Tablets. Marcel Dekker, Inc., New York, 2002; vol 1; 2nd edition: 247-84.
10. MaGruder PR, Barclay B, Wong PSL, Theeuwes F. Composition comprising salbutamol. US Patent. 1988; 4,751,071.
11. Culter N, Anders R, Stanford S, Stramed J, Awan N, Bultas J, Lahari A, Woroszylska M. Placebo-controlled evaluation of three doses of a controlled-onset, extended release formulation of verapamil in the treatment of stable angina pectoris. Am J Cardiol 1995;75:1102–1106.

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https://doi.org/10.71193/jmct.20260017
Journal Home Page: Journal of Medicinal Chemistry and Therapeutics

12. Ueda S, Hata T, Asakura S, Yamaguchi H, Ueda Y. Development of a novel drug release system, time controlled explosion system (TES). Part 1. Concept and design. J Drug Target 1994;2:35–44.
13. Narisawa S, Nagata M, Hirakawa Y, Kobayshi M, Yoshino H. An organic acid-induced sigmoidal release system for oral controlled release preparations. Permeability enhancement of Eudragit RS coating led by the physicochemical interaction with organic acid. J Pharm Sci 1996;85:184–188.
14. Jantzen GM, Robinson JR. Sustained and controlled release drug delivery system. In BankerGS, Rhodes CT, editors. Modern pharmaceutics. 3rd edition New york: Marcel dekkerInc;1996.p.575-09
15. Vyas S,P, Khar RK.Controlled Drug delivery: Concepts and Advances .Concepts and Advances.1st ed.vallabh prakashan,2002,p,156-189.
16. Shargel L,Yu ABC. Modified release drug products. In:Applied Biopharmaceutics and Pharmacokinetics.4th ed.Mc Graw Hill.1999;169-171.
17. Longo WE, Vernava AM III. Prokinetic agents for lower gastrointestinal motility disorders. Dis Colon Rectum 1993;36:696-708.
18. Champion MC, Hartnett M, Yen M. Domperidone, a new dopamine antagonist. Can Med Assoc J 1986;135:457-61.
19. Heykants J, Hendriks R, Meuldermans W, Michiels M, Scheygrond H, Reyntjens H. On the pharmacokinetics of domperidone in animals and man. IV. The pharmacokinetics of intravenous domperidone and its bioavailability in man following intramuscular, oral and rectal administration. Eur J Drug Metab Pharmacokinet 1981;6:61-70.
20. Michiels M, Hendriks R, Heykants J. On the pharmacokinetics of domperidone in animals and man. II. Tissue distribution, placental and milk transfer of domperidone in the Wistar rat. Eur J Drug Metab Pharmacokinet 1981;6:37-48.
21. Association for Consumer Research. Domperidone: an alternative to metoclopramide. Drug Ther Bull 1988;26:59-60.
22. Janssen P, Harris MS, Jones M, Masaoka T, Farré R, Törnblom H, Van Oudenhove L, Simrén M, Tack J (September 2013). "The relation between symptom improvement and gastric emptying in the treatment of diabetic and idiopathic gastroparesis". The American Journal of Gastroenterology. 108 (9): pp1382–91.
23. Bor, S.; Demir, M.; Ozdemir, O.; Yuksel, K. A meta-analysis on the cardiac safety profile of domperidone compared to metoclo pramide. United Eur. Gastroenterol. J. 2018, 6, 1331–1346.

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https://doi.org/10.71193/jmct.20260017
Journal Home Page: Journal of Medicinal Chemistry and Therapeutics

24. Data on file. Janssen Pharmaceutica Inc., Titusville, NJ.
25. Cheer SM, Prakash A, Faulds D, Lamb HM. Pantoprazole: an update of its pharmacological properties and therapeutic use in the management of acid-related disorders. Drugs. 2003;63:101–133.
26. Shi S, Klotz U. Proton pump inhibitors: an update of their clini cal use and pharmacokinetics. Eur J Clin Pharmacol. 2008;64: 935–951.
27. Sachs G. Proton pump inhibitors and acid-related diseases. Pharmaco theraphy. 1997;17:22–37.
28. Sachs G. Proton pump inhibitors and acid-related diseases. Pharmacotherapy 1997; 17 (1): 22-37
29. Huang J-Q, Hunt RH. Pharmacological and pharmacodynamic essentials of H2-receptor antagonists and proton pump inhib itors for the practising physician. Best Pract Res Clin Gas troenterol 2001 Jun; 15 (3): 355-70
30. Kromer W, Kruger U, Huber R, et al. Differences in pH dependent activation rates of substituted benzimidazoles and biological in vitro correlates. Pharmacology 1998 Feb; 56 (2): 57-70
31. Kromer W. Similarities and differences in the properties of substituted benzimidazoles: A comparison between pantopra zole and related compounds. Digestion 1995;56:443±54
32. Cassell D. GERD fighter. New proton pump inhibitor, used widely abroad, ready to enter the marketplace here [editorial]. Drug Topics. 2000;February 21:20.
33. Cheer SM, Prakash A, Faulds D, et al. Pantoprazole: an update of its pharmacological properties and therapeutic use in the management of acid-related disorders. Drugs 2003; 63 (1): 101-33
34. Bharate, S. S., Bharate, S. B., & Bajaj, A. N. (2010). Interactions and incompatibilities of pharmaceutical excipients with active pharmaceutical ingredients : a comprehensive, 1(3), 3–26.
35. Simon Gaisford, Mark Saunders, November 2012 Essentials of Pharmaceutical Preformulation
36. Balestrieri, F., Magri, A. D., Magri, A. L., Marini, D., & Sacchini, A. (1996). Application of differential scanning calorimetry to the study of drug-excipient compatibility, 285, 337–345.
37. Bansal A. K, Macheras P, Preformulation Studies in Drug Development European Journal of Pharmaceutical Sciences, 2008:34(1):1-13

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https://doi.org/10.71193/jmct.20260017
Journal Home Page: Journal of Medicinal Chemistry and Therapeutics

635 38. Patel D, Patel M, Preformulation Studies of New Drug Molecules, International Journal of
636 Research in Pharmaceutical and Biomedical Sciences, 2013:4(2):401-409
637 39. Trambadiya, D.; Bhadani, M.; Shah, K. FORMULATION AND EVALUATION OF FAST
638 DISINTEGRATING METOPROLOL SUCCINATE SUBLINGUAL TABLETS.
639 *PHARMA Sci. Monit. Int. J. Pharm. Sci.* **2013**, *4*, 3975.
640 40. Jamakandi, V. G.; Kubasad, K. A.; Kundu, S.; Dasankoppa, F. S. Design, Formulation, and
641 Evaluation of Delayed Release Oral Dosage Form of Proton Pump Inhibitor. *Indian J.*
642 *Health Sci. Biomed. Res. Kleu* **2016**, *9* (3)
643 41. Bharate, S. S., Bharate, S. B., & Bajaj, A. N. (2010). Interactions and incompatibilities of
644 pharmaceutical excipients with active pharmaceutical ingredients : a comprehensive, 1(3),
645 3–26.
646 42. Balestrieri, F., Magri, A. D., Magri, A. L., Marini, D., & Sacchini, A. (1996). Application
647 of differential scanning calorimetry to the study of drug-excipient compatibility, 285, 337–
648 345.
649 43. Contents, P. O. F. (n.d.). DRUG-EXCIPIENT COMPATIBILITY STUDIES, (166).
650 44. Megarry, A.; Taylor, A.; Gholami, A.; Wikström, H.; Tajarobi, P. Twin-Screw Granulation
651 and High-Shear Granulation: The Influence of Mannitol Grade on Granule and Tablet
652 Properties. Int. J. Pharm. 2020, 590, 119890.
653 https://doi.org/10.1016/j.ijpharm.2020.119890.
654 45. Kleinebudde, P. Application of Low Substituted Hydroxypropylcellulose (L-HPC) in the
655 Production of Pellets Using Extrusion/Spheronization. Int. J. Pharm. 1993, 96 (1), 119–
656 128. https://doi.org/10.1016/0378-5173(93)90219-6.
657 46. Martínez-Acevedo, L.; Galindo-Pérez, M. J.; Vidal-Romero, G.; Real, A. del; Zambrano-
658 Zaragoza, M. de la L.; Quintanar-Guerrero, D. Effect of Magnesium Stearate Solid Lipid
659 Nanoparticles as a Lubricant on the Properties of Tablets by Direct Compression. Eur. J.
660 Pharm. Biopharm. 2023, 193, 262–273. https://doi.org/10.1016/j.ejpb.2023.11.004.
661 47. Van Nguyen, H.; Baek, N.; Lee, B. J. Enhanced Gastric Stability of Esomeprazole by
662 Molecular Interaction and Modulation of Microenvironmental pH with Alkalizers in Solid
663 Dispersion. Int. J. Pharm. 2017, 523 (1), 189–202.
664 48. Hazdi, S. N.; Phang, H. C.; Ng, Z. Q.; Chew, Y. L.; Uddin, A. H.; Sarker, Z. I.; Liew, K.
665 B. Development of a Novel Co-Processed Excipitient Comprising of Xylitol, Mannitol,
666 Microcrystalline Cellulose, and Crospovidone for the Compounding of Memantine
667 Hydrochloride Orally Disintegrating Tablet. Int. J. Pharm. Compd. 2023, 27 (6), 522–527.

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https://doi.org/10.71193/jmct.20260017
Journal Home Page: Journal of Medicinal Chemistry and Therapeutics

668 49. Dzoagbe, H. Y.; Shende, A. S.; Sheikh, M.; Deshmukh, M. Advances in Co-Processed
669 Excipients: Multifunctional Platforms for Diverse Pharmaceutical Formulations. Int. J.
670 Pharm. Investig. 2024, 15 (1), 67–77.
671 50. Kumar, P. FORMULATION AND EVALUATION OF BUCCAL TABLET
672 RABEPRAZOLE SODIUM. *Int. J. Creat. Res. Thoughts IJCRT* **2020**, *8* (10), 2963–2995.
673 51. United States Pharmacopeia Convention. *USP <711> Dissolution*; 711; United States
674 Pharmacopeia (USP), 2023.
675 52. Michael E. Aulton's pharmaceutics: the design and manufacture of medicines. 3rd ed.
676 London: Churchill Livingstone; 2007
677 53. Aulton ME, Taylor K. *Aulton's Pharmaceutics: The Design and Manufacture of Medicines*.
678 5th ed. Elsevier; 2017.
679 54. ICH Q1A(R2). *Stability Testing of New Drug Substances and Products*. International
680 Conference on Harmonisation; 2003.
681 55. Sood A, Panchagnula R. Formulation of a stable enteric coated Pantoprazole tablet:
682 Optimization using factorial design. *Drug Dev Ind Pharm.* 2003;29(4):383-397.
683 56. Zhang G, Law D, Schmitt EA, Qiu Y. Phase transformation considerations during process
684 development and manufacture of solid oral dosage forms. *Adv Drug Deliv Rev.*
685 2004;56(3):371-390.
686 57. Bhowmik BB, Majumder M. Formulation of gastro-resistant Pantoprazole sodium tablets
687 using natural and synthetic superdisintegrants. *J Appl Pharm Sci.* 2011;1(9):103-108.
688 58. Patel DJ, Patel NV, Shah RR. Formulation and evaluation of immediate release tablet of
689 Domperidone and Pantoprazole. *Int J Pharm Sci Res.* 2013;4(1):223-229.
690 59. Allen LV, Popovich NG, Ansel HC. *Ansel's Pharmaceutical Dosage Forms and Drug*
691 *Delivery Systems*. 10th ed. Lippincott Williams & Wilkins; 2013.
692 60. Lachman L, Lieberman HA, Kanig JL. *The Theory and Practice of Industrial Pharmacy*.
693 3rd ed. Lea & Febiger; 1986.
694 61. Thapa P, Jeong SH. Effects of formulation and process variables on tablet properties. *Int*
695 *J Pharm Investig.* 2014;4(1):16-24.
696 62. United States Pharmacopeia and National Formulary (USP 43–NF 38). Rockville, MD:
697 United States Pharmacopeial Convention; 2020.
698 63. Bhagat PR, Salunkhe KS. Studies on the degradation of Pantoprazole sodium and
699 stabilization by using alkalizers. *Int J Pharm Pharm Sci.* 2014;6(1):311-317.
700 64. BP 2020. *British Pharmacopoeia*. London: The Stationery Office; 2020.

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https://doi.org/10.71193/jmct.20260017
Journal Home Page: Journal of Medicinal Chemistry and Therapeutics

65. Rowe RC, Sheskey PJ, Quinn ME. *Handbook of Pharmaceutical Excipients*. 6th ed. Pharmaceutical Press; 2009.
66. Kawtikwar PS, Sakarkar DM, Khadabadi SS. Formulation, evaluation and stability studies of enteric coated Pantoprazole tablets. *J Pharm Res.* 2008;1(2):183-187.
67. Jain R, Jain SK, Jat RC. Development and evaluation of gastro-resistant tablets of Pantoprazole sodium using pH sensitive polymers. *Int J Drug Dev Res.* 2011;3(1):293-301.
68. Banker GS, Rhodes CT. *Modern Pharmaceutics*. 4th ed. Marcel Dekker; 2002.
69. Wagh MP, Gattani SG, Surana SJ. *Pharmaceutical Coating Technology*. In: Jain NK, editor. *Advances in Controlled and Novel Drug Delivery*. CBS Publishers; 2001. p. 74-99.
70. ICH Q1E. *Evaluation of Stability Data*. International Conference on Harmonisation; 2003.

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https://doi.org/10.71193/jmct.20260017
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