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Research Article

Development and Evaluation of Immediate Release Dosage Forms of Antimicrobials for Treatment of *H. Pylori* Infection

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ABSTRACT

A novel therapy comprising of an antibiotic a prostaglandin analogue in modified release dose form that would be an effective treatment for eradication of *H. pylori* infection. *Helicobacter pylori* (*H. pylori*) infection is highly associated with the occurrence of gastrointestinal diseases, including gastric inflammation, peptic ulcer, gastric cancer, and gastric mucosa-associated lymphoid-tissue lymphoma. Although alternative therapies, including phytomedicines and probiotics, have been used to improve eradication, current treatment still relies on a combination of antimicrobial agents, such as amoxicillin. The proposed therapy with immediate release of these drug could prove an effective treatment strategy for *H. pylori* infection in which reduces the inflammation and pain, drug inhibits the bacterial growth suppresses the acid secretion in stomach.

Keywords: H. pylori, Bacterial infection

Introduction:

Infection with H. pylori occurs worldwide, but the prevalence varies greatly among countries and among population groups within the same country [1]. The overall prevalence of H. pylori infection is strongly correlated with socioeconomic conditions [2]. H. pylori cause continuous gastric inflammation in virtually all infected persons. This inflammatory response initially consists of the recruitment of neutrophils, followed by T and B lymphocytes, plasma cells, and macrophages, along with epithelial-cell damage [3]. H. pylori infection can be diagnosed by noninvasive methods or by endoscopic biopsy of the gastric mucosa; the selection of the appropriate test depends on the clinical setting. Noninvasive methods include the urea breath test, serologic tests, and stool antigen assays [4]. The goal of H. pylori treatment is the complete elimination of the organism. Once this has been achieved, reinfection rates are low; thus, the benefit of treatment is durable. Clinically relevant H. pylori– eradication regimens must have cure rates of at least 80 percent (according to intention-to-treat analysis) without major side effects and with minimal induction of bacterial resistance. Such goals have not been achieved with antibiotics alone. Because luminal acidity influences the effectiveness of some antimicrobial agents that are active against H. pylori, antibiotics are combined with proton-pump inhibitors or ranitidine bismuth citrate. So-called triple therapies, combinations of one antisecretory agent with two antimicrobial agents for 7 to 14 days, have been extensively evaluated, and several regimens have been approved by the Food and Drug Administration (FDA). The combination of two or more antimicrobial agents increases rates of cure and reduces the risk of selecting for resistant H. pylori [5]. H. pylori infection is highly associated with gastrointestinal diseases, including gastric inflammation, peptic ulcer, gastric cancer, and gastric mucosa-associated lymphoid-tissue lymphoma [6-7]. It has been classified as a group 1 carcinogen (i.e., infection with H. pylori is carcinogenic in humans) by the International Agency for Research on Cancer consensus group since 1994 [8] and many guidelines have been established for treatment of H. pylori infection [9-10]. The objective of the project is to develop a stable and robust formulation of coating technology of the selected antibiotics over core tablet of proton pump inhibitor (PPI). Regimens for eradication of Helicobacter pylori infection are typically chosen empirically, on the basis of regional bacterial resistance patterns, local recommendations, and drug availability. Therapy for H pylori infection has undergone major changes, based on application of the principles of antimicrobial stewardship

and increased availability of susceptibility testing. Here sustained release formulation avoids the side effects & also provides effects for longer period of time. Sustained release dosage forms provide a dosing of the drug from the product by supplying an initial amount (or) loading dose, perhaps one-half of the total dose release, followed by a gradual and uniform release of the remainder drug over the desired time period and Sustained release dosage form are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose [11].

Material and Methods

Determination of absorption maxima (λ_{max}): The absorption maxima of drug separately were determined by scanning drug solution in double beam ultraviolet spectrophotometer between 200 to 400 nm wavelengths at dissolution medium (phosphate buffer pH 1.2) solution. Accurately weighed required quantity of drug 50 mg drugs individually was dissolved in 50 ml of dissolution medium containing Phosphate buffer pH 1.2 in 50 ml volumetric flask with the help of sonication in bath sonicator for 20 min to obtain 1000 µg/ml solution. From resulting solution take 1 ml and was diluted up to 100 ml with Phosphate buffer pH 1.2 solvent separately with sonication for 20 min to get 10 µg / ml solution with the help of methanol in 10 ml volumetric flasks. The spectrum of these solutions was run in 200 – 400 nm range in double beam UV spectrophotometer (Shimadzu, UV-1800, Shimadzu Corporation, Kyoto, Japan).

Preparation of calibration curve: Accurately weighed required quantity of drug 50 mg separately were dissolved in 50 ml of dissolution medium containing Phosphate buffer pH 1.2 in 50 ml volumetric flasks with the help of sonication in bath sonicator for 20 min to obtain 1000 µg/ml solution. From resulting solution take 10 ml and was diluted up to 100 ml with Phosphate buffer pH 1.2 solvent separately with sonication for 20 min to get 100 µg / ml solution. From above prepared resulting solution of 100 µg / ml, withdrawn 0.5 ml, 1.0 ml, 1.5 ml upto 4.0 ml aliquots and diluted up to 10 ml with respective solvent (Phosphate buffer pH 1.2) in 10 ml volumetric flasks to get concentration of 5 µg / ml, 10 µg / ml, 15 µg / ml, upto 40 µg / ml respectively. The absorbance of each solution was measured separately at 273 nm for amoxicillin [12].

Preformulation study of drugs:

Organoleptic properties*:* The organoleptic properties of drug (amoxicillin and omeprazole) separately were determined such as color, odor and taste will be noted visually.
Microscopic examination: The microscopic examination of the drug samples (amoxicillin and omeprazole) separately was identified the nature / texture of the powder. The required amount of powder will spread on a glass slide and examine under phase contrast microscope.
Density: The drug powders (amoxicillin and omeprazole) separately were weighed accurately and kept through a glass funnel into graduated cylinder. During this experiment the volume will note and bulk density will be determined.
Particle size: The average particle size (d_{avg}) of drug powders (amoxicillin and omeprazole) separately were determined by means of optical microscope fitted with ocular micrometer and stage micrometer.
Flow properties: The flow properties of drug powders (amoxicillin and omeprazole) separately were were characterized in terms of carr's index, hausner's ratio and angle of repose. The Carr's index ((I_C)) and Hausner's ratio (H_R) of drug powders were calculating according to following equation:
Carr's Index (I_C) = $\rho_{Tapped} - \rho_{Bulk} / \rho_{Tapped}$
Hausner's ratio (H_R) = $\rho_{Tapped} / \rho_{Bulk}$
The angle of repose (θ) was measured by fixed height method. This was calculated by following equation:
Angle of repose (θ) = $\tan^{-1}$ 2 H / D
Where H is the surface area of the free-standing height of the powder pile and D is diameter of pile that formed after powder flow from the glass funnel.
Solubility determination: Saturation solubility of drug API (amoxicillin and omeprazole) separately were determined by incremental method analysis method in various solvents. The exact quantity of drug 50 mg was placed on the conical flask and the various solvents i.e. distilled water, 0.1 N HCl, Phosphate buffer pH 6.8 and pH 7.4 phosphate buffers separately filled in burette. The solvent was slowly added into drug containing conical flask until the drug was solubilized and stirred constantly overnight at 37±0.5°C. The samples were filtered by using whatmann filter paper (0.45µm pore size). The solubility assessment of drug was determined by calculation of concentration µg/ml unit.
Partition coefficient: The partition coefficient of drug samples (amoxicillin and omeprazole) separately were observed in mixed solvent of 100 ml containing n-octanol: phosphate buffer pH 1.2. 100 mg of drug was added into 50 ml each of an n-octanol and buffer phase in a separating funnel. The mixture was shaken for 24 h until equilibrium reached. Both medium were divided and collected individually, filtered. The quantity of API dissolved in aqueous medium was diluted and determined by UV spectrophotometric method. The partition coefficient of API was calculated from the proportion between the concentrations of drug in organic and buffer solution quantity using following equation.
Log $P_{(oct / pH\ 1.2)}$ = Log ($C_{noct} - C_{pH1.2}$) equilibrium

Melting point: The melting point of drug samples (amoxicillin and omeprazole) separately were were obtained by pinch of drug material sample filled in capillary tube by manually. Capillary tube sealed from one end with a bunsen flame burner individually. The filled capillary tube was kept in melting point apparatus and identified the temperature at which the drug was starting to melt.

Drug excipient compatibility study: The functional group determination of drug samples (amoxicillin and omeprazole) separately were identified by IR spectroscopy. Infra-red spectroscopy was carried out by using Shimadzu IR Spectra photometer as method given below. The characteristic peaks were reported as wave number. The FTIR spectra of dried drug samples (amoxicillin and omeprazole) independently were obtain by FTIR spectrophotometer by means of the potassium bromide disc method. The drug sample was pulverized and thoroughly mixed with a dried powder of IR grade potassium bromide material with weight ratio of 3:1 (i.e 9 mg of KBr in 1 mg of drug). The mixture of materials was pressed using a hydrostatic press at a pressure of 10 tons for 5 min at room temperature with required humidity. The disc of sample was placed in the sample holder for measuring the spectrum and the spectra were recorded as the wave number ranges 4000-400/cm at a resolution of 4/cm. The compatibility i.e. drug-excipients interaction studies are helpful for dosage form design. For compatibility studies drug / excipients ratio are selected and investigated based on the reasonable drug / excipient ratio in the final product. Drug and other Excipients were weighed as 1:1 ratio and passed through sieve # 40, mixed well. The blend was filled in amber color glass vials and stopped with grey rubber stoppers followed by aluminium seal [13].

Formulation of immediate release tablets: Weighed quantity of drug omeprazole 20mg, pregelatinized starch, and croscarmellose sodium (half quantity) was passed through # 40 mesh and mixed cage blender for 10 minutes at 20 rpm. Accurately weighed PVP K-30 and sodium lauryl sulfate was dissolved in purified water to prepare a binder solution. Granules were prepared from the blend, dried and size reduced. Accurately weighed croscarmellose sodium (remaining half quantity), avicel PH 102 and Aerosil were passed through a sieve. Iron oxide red was weighed, passed through a sieve, and mixed with extra granular material. Finally prepared granules were lubricated by sodium stearyl fumarate (SSF). After evaluation of pre-compression parameters, compression into 90 mg tablets using flat-faced, round punches 4 mm in diameter [14].

Evaluation of immediate released tablets:

Flow properties:

Angle of repose: A weighed quantity of microspheres was passed through a funnel fixed on a stand at a specific height upon a graph paper. A static heap of powder with only gravity acting upon it was tending to form a conical mound. The height of the heap (h) and radius (r) of lower part of cone were measured and calculated.

$\theta = \tan\text{-}1h/r$

where θ = angle of repose, h = height of cone and r = radius of cone base

Carr's index: The Carr's index was evaluated for the flow ability of the powder by comparing the pour density and tapped density of microspheres and was calculated using:

Carr's index = $\{(\rho t\text{-}\rho b) \times 100\}/\rho t$

where ρb is bulk density and ρt is tapped density which was measured in a 10ml graduated cylinder and the number of tapings was 100 as it was sufficient to bring about a plateau condition. Carr's index less than 15 % gives good flow characteristics and above 25 % indicates poor flow characteristics

Hausner's ratio: Hausner's ratio (H), another index of flow ability, was calculated using:

$H = \rho t/\rho b$

A value < 1.2 is preferred for free flow; however, a value close to 1 indicates good flow properties.

Weight variation: The average weight by more than the percent shown below and none deviates by more than twice that percent.

Hardness: Hardness of tablet is defined as the force required to break a tablet a in a diametric direction. A tablet was placed between two anvils. Hardness is thus the tablet crushing strength. Monsanto tester is used for hardness testing.

Friability: Weigh 10 tablets and place in a friabilator chamber rotated at 25 rpm and they are dropped on distance of 6 inches and allowed to rotate for 100 revolutions. The difference in the weigh is calculated and the weight loss should not be more than 1%.

Thickness: The thickness of tablets was performed on 20 tablets from each formulation by using Vernier caliper.

Percent Drug content estimation: Crushed 10 tablets from all batches in pestle-mortar and weighed equivalent 150 mg as drug dose using for single tablet was taken in volumetric flask (100ml) and dissolved in 0.1 N HCL (pH 1.2 phosphate buffer) and filtered. This solution was analyzed in UV spectrophotometer at λmax 225 nm.

***in-vitro* Dissolution study:** In vitro dissolution study was carried out using USP type II (basket type) apparatus with 0.1N HCl (pH 1.2 phosphate buffer) as a dissolution medium. The temperature was maintained at 37±0.5°C with 50 rotations per minute. 1ml of aliquots were withdrawn at different time intervals and same amount of fresh dissolution medium was replaced to maintain sink condition. The

aliquots were analyzed for drug content at λ max 225 nm wavelength using UV-spectrophotometer. The cumulative percentage drug release was calculated and reported.

***in-vitro* drug release kinetic study:** The drug release and mechanism release can be determined by matching the data with various release models like Higuchi, Korsmeyer-Peppas, zero order and first order plots. The kinetics of drug release was studied in various kinetic models by plotting the data obtained from in vitro drug release study. The zero-order kinetics was studied by plotting cumulative amount of drug released versus time. Whereas first order kinetics was studied by plotting log cumulative percentage of drug remain versus time. Higuchi's model of kinetics was studied by plotting cumulative percentage of drug released versus square root of time. The mechanism of drug release from the formulation was confirmed by fitting the in vitro drug release data with the Korsmeyer–Peppas model by plotting log cumulative percentages of drug release versus log time. The release exponent 'n' and 'k' values were calculated from the Y intercept and slope of a straight line respectively [15]

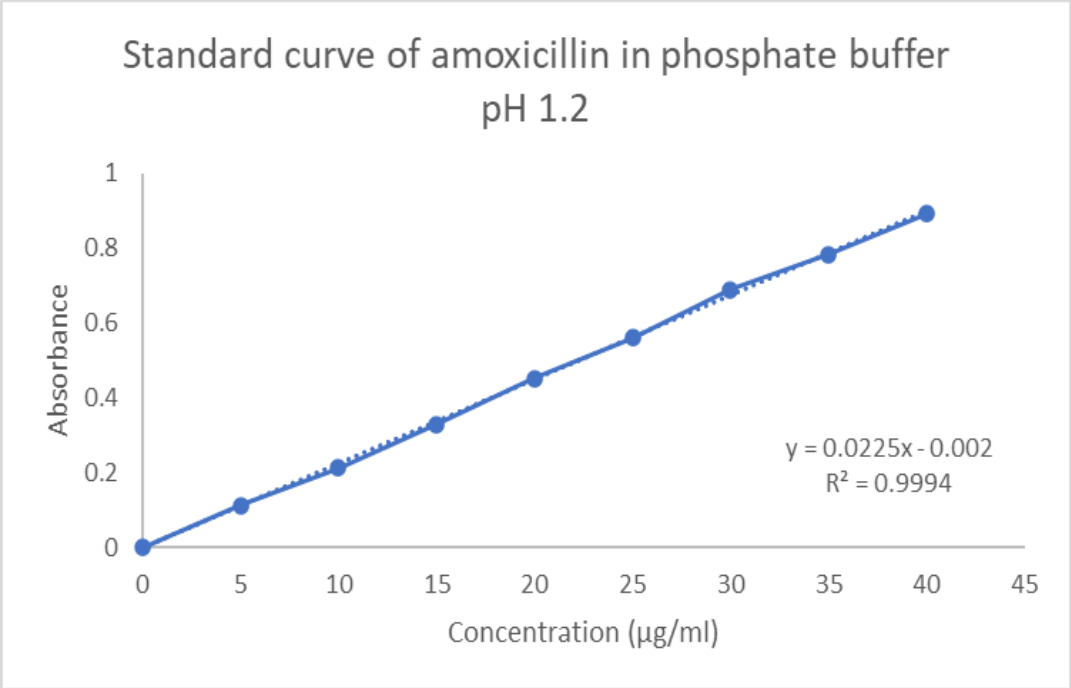

Figure 1: Standard curve of amoxicillin in phosphate buffer pH 1.2 (225 nm)

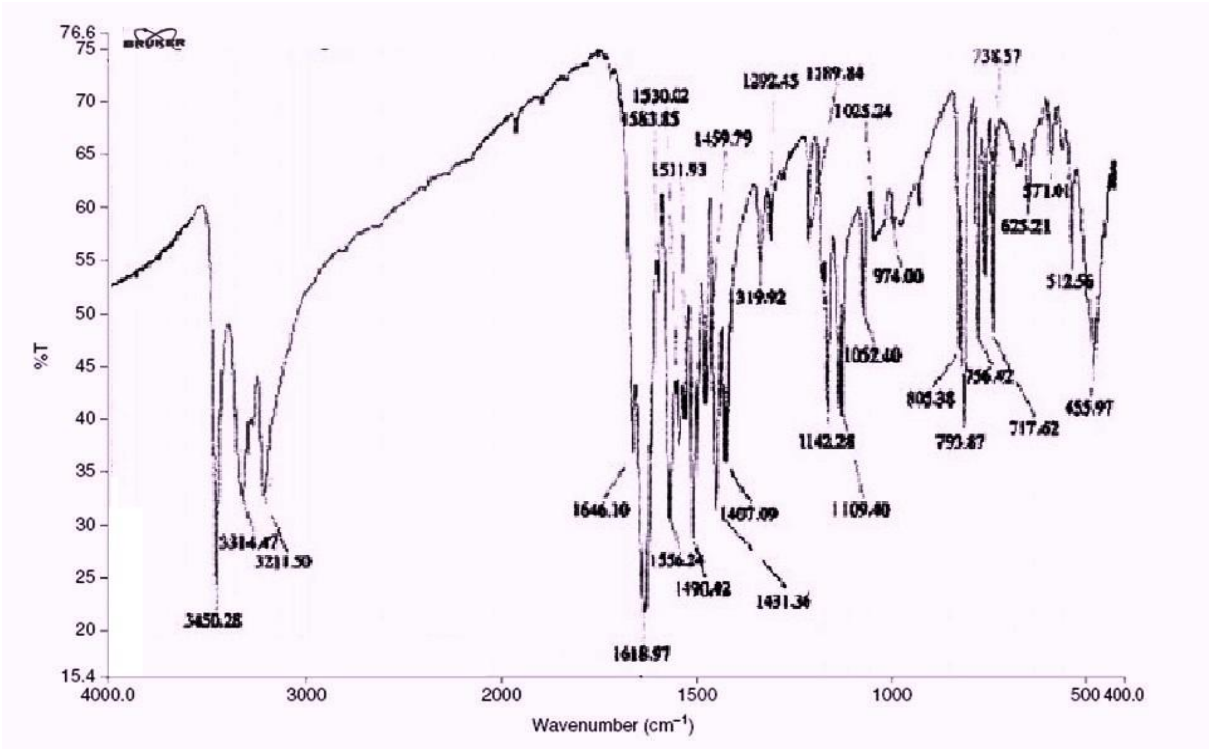

Figure 2: The I. R. Spectrum of amoxicillin sample (S1)

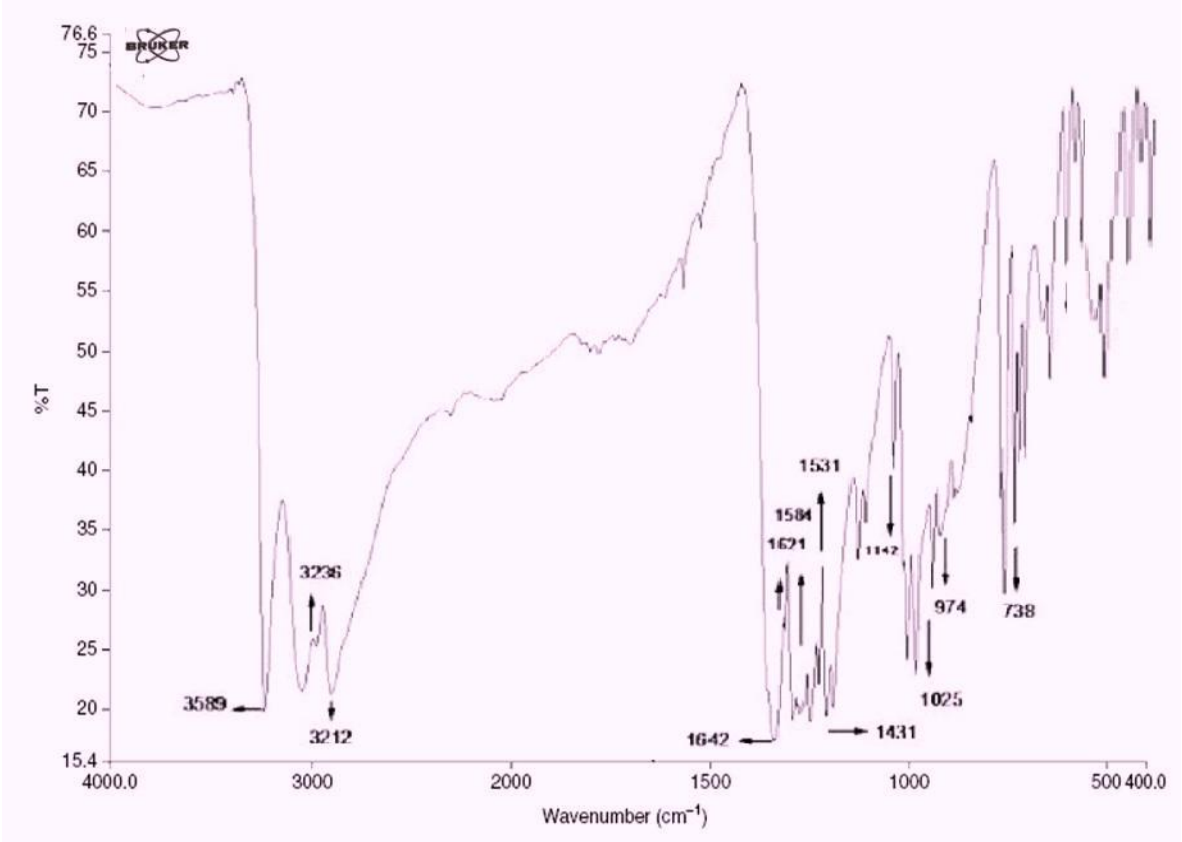

Figure 3: The I. R. Spectrum of amoxicillin drug and all excipient (S2)

Table 1: Composition of omeprazole tablet prepared by wet granulation method

Ingredients	Amount (mg / tablet)								
	OIR1	OIR2	OIR3	OIR4	OIR5	OIR6	OIR7	OIR8	OIR9
Omeprazole (mg)	20	20	20	20	20	20	20	20	20
Microcrystalline cellulose (Avicel pH 102)	50	50	50	50	50	50	50	50	50
Di basic calcium Phosphate dihydrate (DBP)	30	40	50	60	70	45	40	35	30
Lactose anhydrous	100	90	80	70	60	70	80	90	100
Potato Starch	-	-	-	-	-	30	25	20	15
Sodium starch glycollate	15	15	15	15	15	-	-	-	-
Purified Talc	5	5	5	5	5	5	5	5	5

Table 2: Flow properties of various precomprerssed granules

Formulation code	Bulk density (g/cc)	Tapped density (g/cc)	Carr's index (%)	Hausner Ratio	Angle of Repose
OIR1	0.149	0.133	15.63	1.12±0.021	24.1±0.187
OIR2	0.176	0.167	16.45	1.23±0.015	24.5±0.102
OIR3	0.165	0.158	13.45	1.16±0.012	24.1±0.103
OIR4	0.162	0.153	15.35	1.19±0.011	26.3±0.112
OIR5	0.169	0.158	14.63	1.16±0.011	22.1±0.102
OIR6	0.171	0.161	14.21	1.13±0.011	23.4±0.111
OIR7	0.168	0.161	15.12	1.19±0.012	22.9±0.121
OIR8	0.173	0.164	16.02	1.15±0.014	23.8±0.131
OIR9	0.168	0.162	14.25	1.21±0.021	25.2±0.114

Table 3: The various characterization of omeprazole immediate release tablet

Formulation code	Bulk density (g/cc)	Tapped density (g/cc)	Carr's index (%)	Hausner Ratio	Angle of Repose
OIR1	0.149	0.133	15.63	1.12±0.021	24.1±0.187
OIR2	0.176	0.167	16.45	1.23±0.015	24.5±0.102
OIR3	0.165	0.158	13.45	1.16±0.012	24.1±0.103
OIR4	0.162	0.153	15.35	1.19±0.011	26.3±0.112
OIR5	0.169	0.158	14.63	1.16±0.011	22.1±0.102
OIR6	0.171	0.161	14.21	1.13±0.011	23.4±0.111
OIR7	0.168	0.161	15.12	1.19±0.012	22.9±0.121
OIR8	0.173	0.164	16.02	1.15±0.014	23.8±0.131
OIR9	0.168	0.162	14.25	1.21±0.021	25.2±0.114

Table 4: The various characterization of omeprazole immediate release tablet

Formulation code	Weight variation (mg)	Thickness (cm)		Hardness (kg/cm²)	Friability (%)	Disintegration Time (sec)	Percent Drug content (%)
		Diameter	Thickness				
OIR1	122.9±1.00	0.111±0.003	0.028±0.002	5.27	0.44	61.04	98.2±0.89
OIR2	127.6±1.22	0.113±0.002	0.031±0.002	5.29	0.45	51.11	98.8±1.01
OIR3	123.6±1.80	0.110±0.001	0.031±0.001	5.28	0.43	69.18	98.1±1.22
OIR4	127.6±1.75	0.112±0.001	0.029±0.001	5.29	0.49	41.11	98.7±0.92
OIR5	123.5±1.26	0.113±0.001	0.029±0.001	5.32	0.47	68.12	98±0.58
OIR6	119.2±1.17	0.111±0.002	0.031±0.002	5.27	0.42	61.08	98.7±0.09
OIR7	121.1±1.01	0.112±0.003	0.031±0.002	5.38	0.46	66.16	98.4±0.11
OIR8	124.3±1.02	0.110±0.002	0.029±0.003	5.34	0.43	65.15	98.6±0.13
OIR9	126.2±1.21	0.112±0.002	0.028±0.002	5.29	0.47	61.11	98.3±0.12

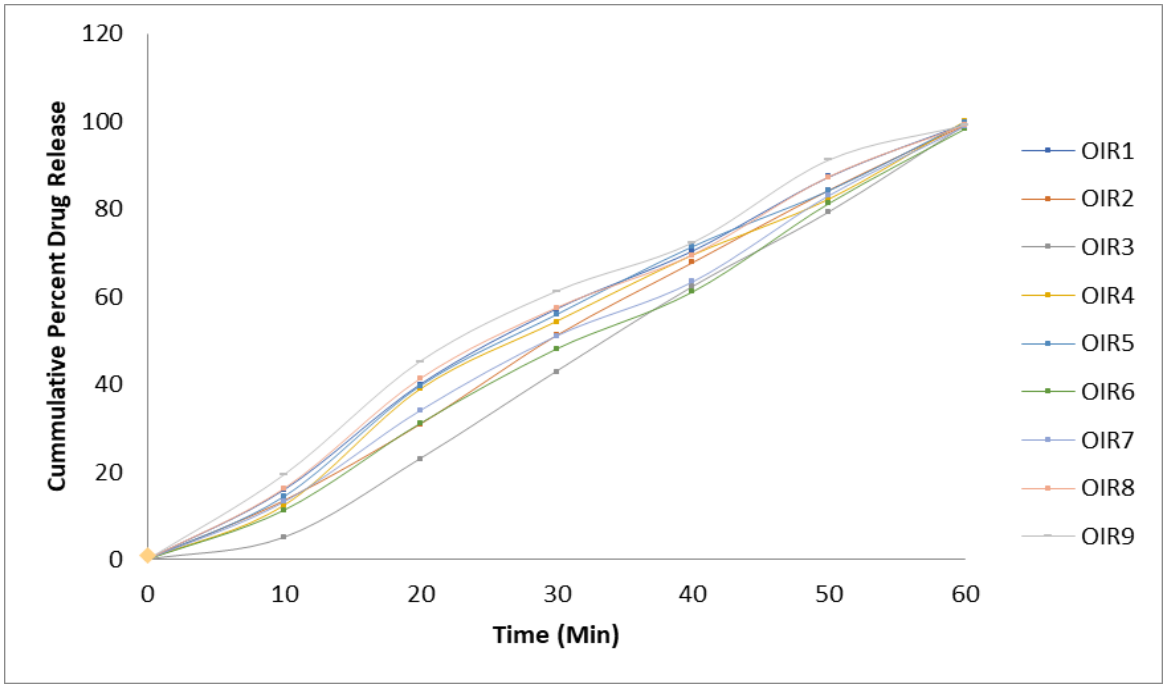

Figure 4: Zero-order kinetic plot of the prepared various omeprazole immediate release tablet (OIR1-OIR9)

Results And Discussion: The absorption maxima (λ-max) of amoxicillin (10 µg / ml) in pH 1.2 solution were found to be at 225 nm. The absorbance of the resulting solution was measured at λmax 225 nm for drug amoxicillin against a blank solution prepared similarly without drug using systronics double beam spectrophotometer. Calibration curve was prepared by plotting concentration versus absorbance. Preformulation studies are the first step for the rational development of dosage forms of model drug substances. It is an investigation of physical and chemical properties of drug substances alone and in combination with excipients in research. The overall objective of preformulation studies is to produce

information constructive to the formulator in development of stable and bioavailable dosage forms. Amoxicillin is pale cream-colored, odorless, slightly bitter and crystalline powder in nature and omeprazole is white colored, fishy smell, bitter and crystalline powder in nature. The bulk and tapped density of drug amoxicillin 0.881 gm / cm^3 and 0.921gm / cm^3, respectively. The particle size of unmilled amoxicillin was to be 29.7 µm. Drug powder exhibited good flow characteristics. The drug amoxicillin has carr's index 26.01±0.61, hausner's ratio 1.13±0.012 and angle of repose θ 24.2°±0.16. The solubility of drug amoxicillin was determined in various solvents (Water, 0.1 N HCl, Phosphate buffer pH 4.5, pH 6.8, pH 7.4) at room temperature (25±2 ºC). The solubility in water 241.5±9.21 (µg / ml), 0.1 N HCl 1089.0±27.91 (µg / ml), phosphate buffer pH 6.8 331.8±8.32 (µg / ml) and phosphate buffer pH 7.4 302.2±7.87 (µg / ml). The result indicated that the drug has maximum solubility water, and also soluble in pH 1.2 phosphate buffer. The partition coefficient of drug amoxicillin and omeprazole were found to be (1.09). The melting point of drug amoxicillin were found to be 169°C ± 0.12°C. In order to study the interaction between drug amoxicillin and excipients the samples were studied for FTIR detection and physical study. The change in the physical properties of drugs was studied, drug content of the mixtures was determined and IR studies were performed. The FTIR spectrum is shown in Figure 6.5 to 6.6. The characteristic peaks of FTIR spectrum for Lamotrigine (recorded from a KBr pellet) and absorption bands due to Secondary amine N-H stretching at 3275.19 cm -1 and bending at 1597.09 cm -1 . 2. = CH stretching at 3113.16 cm -1 . 3. Acyclic ketone carbonyl (C=O) stretching at 1709.92 cm -1 . 4. SO 2 NH stretching at 1354.05 cm -1 . 5. Sulphonyl S=O stretching at 1164.06 cm -1 . Here, secondary amine (N-H) possesses one band for stretching at 3275.19 cm -1 and one band for bending at 1597.09 cm -1 . were observed.

Pre-compression parameters such as angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio were evaluated for powder blend. The various omeprazole immediate release tablet by solventless coating technology by direct compression coating technology dosage form helps in absorption of the drugs from the upper gastrointestinal tract. The other characterization includes weight variation, thickness, hardness, friability, mechanical strength, measurement of tablet porosity, wetting time and water absorption ratio, moisture uptake studies, in-vitro dispersion time, disintegration test, determination of drug content, *in-vitro* drug release dissolution test, *in-vitro* drug release kinetic study and stability study. The flow properties of powder blend were evaluated in terms of carr's index, hausner's ratio and angle of repose. All the blend powders exhibited good flow properties. The physical properties (i.e., weight, thickness, hardness, friability, water uptake capacity, swelling ratio, disintegration time and drug content) of antidiabetic tab in tablet were studied. The tablet was varied from 0.210 to 0.213 cm in diameter and 0.191 to 0.192 cm in thickness, average weight was varied from 812.9 to 817.6 mg, hardness was varied from 5.22 to 5.32 kg / cm^2, friability was varied from 0.42 to 0.49 %, disintegration time was varied from 1.04 to 1.18 hr and drug content was varied from 98.0 to 98.8 % for for OIR1 to OIR2. The release of drug from the antidiabetic tablets was influenced significantly by the variation of excipents of tablet in dissolution media. This was evidenced by the whole amount of drug released from tablets through direct compression tablets. The preliminary and screening studies were performed using different polymers and the polymers citric acid, sodium bicarbonate, HPMC, promised excellent properties for controlled release and muco-adhesion. Using selected polymers, the final batches were prepared by direct compression method and were evaluated for buoyancy lag time and total buoyant time, swelling index, drug content, ex-vivo mucoadhesive strength, in-vitro dissolution study. The formulation OIR3 was found to be the best formulations in terms of sustained drug release. Drug release kinetics was performed by using various kinetic models such as Zero order, First order, Korsmeyer- Peppas and Higuchi's equation. The regression coefficient (r^2) value of various models was found to be non-fickinon drug release diffusion mechanism and followed supercase II transport mechanism respectively.

Summary And Conclusion: The absorption maxima (λ-max) of amoxicillin (10 µg / ml) in pH 1.2 solution were found to be at 225 nm. Preformulation studies are the first step for the rational development of dosage forms of model drug substances. Amoxicillin is pale cream-colored, odorless, slightly bitter and crystalline powder in nature and omeprazole is white colored, fishy smell, bitter and crystalline powder in nature. The bulk and tapped density of drug amoxicillin 0.881 gm / cm^3 and 0.921gm / cm^3, respectively. The particle size of unmilled amoxicillin was to be 29.7 µm. Drug powder exhibited good flow characteristics. The drug amoxicillin has carr's index 26.01±0.61, hausner's ratio 1.13±0.012 and angle of repose θ 24.2°±0.16. The solubility of drug amoxicillin was determined in various solvents (Water, 0.1 N HCl, Phosphate buffer pH 4.5, pH 6.8, pH 7.4) at room temperature (25±2 ºC). The result indicated that the drug has maximum solubility water, and also soluble in pH 1.2 phosphate bufferThe partition coefficient of drug amoxicillin and omeprazole were found to be (1.09 and 0383) separately. The melting point of drug amoxicillin and omeprazole were found to be 169°C ± 0.12°C and 232°C ± 0.11°C separately. Pre-compression parameters such as angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio were evaluated for powder blend. The various omeprazole immediate release tablet by solventless coating technology by direct compression coating technology dosage form helps in absorption of the drugs from the upper gastrointestinal tract. The other characterization includes weight variation, thickness, hardness, friability, mechanical strength, measurement of tablet porosity, wetting time and water absorption ratio, moisture uptake studies, in-vitro dispersion time, disintegration test, determination of drug content, *in-vitro* drug release dissolution test, *in-vitro* drug release kinetic study and stability study. The flow properties of powder blend were evaluated in terms of carr's index, hausner's ratio and angle of repose. The tablet was varies from 0.210 to

0.213 cm in diameter and 0.191 to 0.192 cm in thickness, average weight was varies from 812.9 to 817.6 mg, hardness was varies from 5.22 to 5.32 kg / cm^2, friability was varies from 0.42 to 0.49 %, disintegration time was varies from 1.04 to 1.18 hr and drug content was varies from 98.0 to 98.8 % for for OIR1 to OIR2. The release of drug from the antidiabetic tablets was influenced significantly by the variation of excipents of tablet in dissolution media. This was evidenced by the whole amount of drug released from tablets through direct compression tablets. The preliminary and screening studies were performed using different polymers and the polymers citric acid, sodium bicarbonate, HPMC, promised excellent properties for controlled release and muco-adhesion. Using selected polymers, the final batches were prepared by direct compression method and were evaluated for buoyancy lag time and total buoyant time, swelling index, drug content, ex-vivo mucoadhesive strength, in-vitro dissolution study. The formulation OIR3 was found to be the best formulations in terms of sustained drug release. Drug release kinetics was performed by using various kinetic models such as Zero order, First order, Korsmeyer- Peppas and Higuchi's equation. The regression coefficient (r^2) value of various models was found to be non-fickinon drug release diffusion mechanism and followed supercase II transport mechanism respectively.

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