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Exploring the synergistic effect in polyherbal chewable antacid tablets: formulation and evaluation study

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ABSTRACT

Polyherbal chewable tablets of *Phyllanthus emblica* and *Glycyrrhiza glabra* were developed with the objective to formulate an effective, safe and convenient dosage form for acid-related disorders. A standard calibration curve was constructed for Polyherbal extracts through UV-Spectrophotometry, achieving an absorbance maximum at 275 nm. Compatibility between the drug and excipients was examined through FTIR studies. Various pre-compression parameters, like bulk density, tapped density, compressibility index, Hausner's ratio and angle of repose, were assessed for the powder blend. The tablets were evaluated for post-compression parameters, such as thickness, hardness, friability, and weight variation and disintegration time. The drug release study was conducted *in vitro*. The acid-neutralizing capacity of the formulated batches was compared with marketed formulations. The calibration curve showed a high correlation coefficient (r^2=0.9972), suggesting accuracy and reliability. FTIR analysis confirmed the compatibility between the drug and excipients. Pre-compression studies revealed an acceptable range for all parameters, indicating good flow properties. For instance, Carr's Index for all batches varied from 14.31% to 24.41%, and the angle of repose ranged from 33.7 to 35.21 degrees. Post-compression parameters were within the standard limits with hardness between 4.9 to 6.1 kg/cm^2 and friability less than 1% for all batches. *In vitro* drug release showed a gradual increase over time with PF9 achieving 98.63% release at 60 min. The acid-neutralization capacity was highest for the combined extract at 27.83±0.34 mEq/g and PF9 batch at 28.12±0.43 mEq/g, demonstrating their effectiveness in neutralizing acid.

The study successfully formulated a Polyherbal chewable tablet with optimized pre and post-compression parameters. The tablet exhibited promising *in vitro* drug release and an efficient acid-neutralizing capacity. It holds potential as an effective treatment option for acid-related disorders.

INTRODUCTION

The escalating use of herbal products in modern healthcare has opened a new vista in pharmaceutical research, underscoring the potential of medicinal plants in the development of effective, safe and affordable drugs. Notably, the formulation of Polyherbal chewable antacid tablets has surfaced as a research area of considerable interest, and this study seeks to delve into the depths of this uncharted territory [1]. The core focus of the present research article is to explore the synergistic effect in Polyherbal chewable antacid tablets, closely examining the formulation process and conducting a detailed evaluation of the outcomes [2].

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Antacids are commonly used medications that help neutralize stomach acid and alleviate symptoms of gastro-esophageal reflux disease (GERD) and peptic ulcers. While most conventional antacids rely heavily on inorganic compounds such as magnesium hydroxide, aluminum hydroxide or calcium carbonate, the advent of herbal antacids has brought about a transformation in treatment methodology. Herbal antacids, constituted from medicinal plants known for their antacid properties, offer a natural and often safer alternative to their chemical counterparts [3].

In this study, we embark on a journey to unravel the formulation intricacies of Polyherbal chewable antacid tablets using two remarkable medicinal plants – *Phyllanthus emblica* (Indian gooseberry or Amla) and *Glycyrrhiza*

glabra (liquorice root). Both of these plants have a rich history of use in traditional medicine, and their therapeutic properties have been well-documented. *Phyllanthus emblica*, a fruit known for its high vitamin C content and robust antioxidant properties, exhibits promising gastroprotective effects. It has been known to enhance the health of the digestive system and alleviate hyperacidity, positioning it as an excellent ingredient for antacid formulation [4]. On the other hand, *Glycyrrhiza glabra*, renowned for its sweet root, is another potent herb employed in managing digestive system disorders. Liquorice root contain glycyrrhizin (glycyrrhizic acid) which is known for its soothing effect on the stomach lining, potentially healing gastric ulcers and mitigating GERD symptoms. Its anti-inflammatory and immune-boosting properties also contribute to its role as a potential ingredient in antacid formulation [5].

By intertwining the potent properties of these two unique herbs, we anticipate creating a synergistic effect that could heighten the antacid efficacy of the formulated tablets. This investigation will employ a rigorous evaluation method, encompassing *in-vitro* and *in-vivo* studies, to ascertain the tablet's properties, stability and effectiveness [6].

In a broader sense, this study is expected to contribute to the realm of pharmaceutical science, offering insights into the synergistic effect of combining multiple herbs in the formulation of chewable antacid tablets. Ultimately, we hope to provide a platform for future research that continues to explore and unlock the therapeutic potential of Nature's pharmacy [7].

MATERIAL AND METHOD

Materials

The primary components for this study were dried extracts of *Phyllanthus emblica* and *Glycyrrhiza glabra*, kindly provided by Konark Herbals and Health Care Pvt. Ltd., Daman. Additional excipients employed in the formulation included Mannitol, Croscarmellose Sodium, Microcrystalline Cellulose (MCC), Vanillin, Talc and Magnesium Stearate. All chemicals and solvents utilized in this research were of analytical grade, ensuring accuracy and reliability in the experimental processes.

Methods

Preparation of Standard Calibration Curve of plants

The preparation of the standard calibration curve began with the creation of a stock solution. A 100 mg quantity of the Polyherbal extract in a 1:1 ratio was dissolved in a small amount of distilled water and then diluted to a volume of 100 mL, producing a concentration of 1000 µg/mL. The absorption maxima for this stock solution were identified within the 200-400 nm range using a UV spectrophotometer. The spectrum of the Polyherbal extract was measured by way of a Shimadzu UV-1800 instrument [8]. Subsequently, the stock solution underwent serial dilution with water to generate concentrations of 5, 10, 15, 20, 25 and 30 µg/mL. The absorbance for each of these concentrations was measured at 275 nm by employing a UV spectrophotometer, with a blank buffer solution serving as the reference. The resulting absorbance values were then plotted against the corresponding concentrations (µg/mL) to create the standard calibration curve for the plant extracts [9].

Preformulation Study

The preformulation study is a critical phase in the research where the compatibility of the drug and excipients is evaluated, and the antacid activity of the individual and combined herbal extracts is assessed [10].

Drug-excipient IR compatibility study

The compatibility of the Polyherbal extracts with the additional excipients used in the formulation of Polyherbal chewable tablets was investigated via Fourier Transform Infrared (FTIR) spectroscopy [11]. FTIR spectroscopy provides valuable insights into the chemical structures of the herbal extracts, thereby enabling us to verify the compatibility of the drug and excipients. Physical mixes of the drug and excipients were prepared in a 1:1 ratio, and then passed through sieve #30. These samples were then placed in sealed, labelled vials and subjected to FTIR analysis using a Potassium Bromide (KBr) sample [12].

Formulation of chewable tablet

In the process of formulating the chewable tablets, each component was carefully weighed individually. Ingredients including *Phyllanthus emblica*, *Glycyrrhiza glabra*, Mannitol, Croscarmellose Sodium, Microcrystalline Cellulose (MCC) and Vanillin were combined in a mortar and pestle and thoroughly mixed for duration of 10 minutes. This blend was then further lubricated with Magnesium Stearate and Talc for an additional 2 minutes [13]. Following this, the flow properties of the powder blend were examined and found to be satisfactory for tablet compression. This optimized blend was then compressed into tablets, each weighing 400 mg, employing a straightforward direct compression method. At least 50 tablets were produced for each batch to ensure statistical validity. The composition for the tablet formulation is detailed in Table 1 [14].

Table 1. The composition of the Chewable tablets for PF1 to PF9

Sr. No.	Formula	Quantity in mg								
		PF1	PF2	PF3	PF4	PF5	PF6	PF7	PF8	PF9
1	*Phyllanthus emblica*	100	100	100	100	100	100	100	100	100
2	*Glycyrrhiza glabra*	100	100	100	100	100	100	100	100	100
3	Mannitol	122	144	124	162	142	153	133	113	104
4	Croscarmellose sodium	2	20	20	2	2	11	11	11	20
5	MCC	60	20	40	20	40	20	40	60	60
6	Talc	8	8	8	8	8	8	8	8	8
7	Vanillin	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
8	Mg. Stearate	8	8	8	8	8	8	8	8	8
Total Weight		400	400	400	400	400	400	400	400	400

Evaluation of Polyherbal chewable tablet

Pre-compression evaluation

Bulk density

In deriving this, 2 g of granules were weighed precisely, then transferred to a 10 mL graduated cylinder after passing

through a 20# sieve. The powder gently was subsequently levelled without compacting it, then the apparent volume (V0) was gauged. Using the following formula, the apparent bulk density in g/ml was determined [15]:

$$\text{Bulk Density} = \frac{\text{Weight of powder}}{\text{Bulk volume}} \quad (1)$$

Tapped density

According to USP II, the sample was initially tapped 10, 500, and 1250 times (strokes). The volume of the tapped sample was measured, and another 1250 tap test was performed. If the volumes at 500 taps (V2) and 1250 taps (V3) deviated by more than 2 ml, the procedure was repeated. The tapped density was calculated using this result. The difference between V1 and V2 was used to calculate the powder's ability to settle [16].

$$\text{Tapped Density} = \frac{\text{Weight of powder}}{\text{Tapped volume}} \quad (2)$$

Carr's Index

The Carrs compressibility index was applied to calculate the compressibility index of the powder mixture, as this is an easy test to perform for determining a powder's BD, TD and agglomeration rate. The following equation was used to calculate the Carrs Index [16]:

$$\text{Carr's Index} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped volume}} \times 100 \quad (3)$$

Hausner's ratio

Hausner's ratio is a number that correlates to the flowability of a powder or granule [17].

$$\text{Hausner's ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}} \quad (4)$$

Angle of repose

The fixed funnel method was used to calculate the angle of repose. The funnel is set at a specific height above the graph paper on a level horizontal surface in this procedure. A precisely weighted amount of powder was poured down the funnel to form a conical mound that touched the funnel's tip. The diameter of the conical heap's base was then estimated in order to compute the angle of repose [18],

$$\Theta = \text{Tan}^{-1} \cdot \frac{h}{r} \quad (5)$$

where, h and r are the height and radius of the powder cone, respectively.

Post-compression evaluation

Thickness and diameter

Using a micrometre, the thickness of each tablet was measured. This approach allowed for a precise measurement and revealed the variation between tablets [18].

Hardness

The breaking strength of a tablet indicates the hardness of the tablet. This may be brought on by the powder's poor flow characteristics or moisture content. The hardness of the tablets was examined using a Monsanto hardness tester [19].

Friability

Twenty tablets were randomly selected from each batch and weighed. These tablets were tested for friability using a friabilator (of the Roche type) for 100 rotations (25 rpm for four min.) The tablets were then taken out, dusting off and then reweighed. SD was calculated using average triplicate readings that were recorded [19].

$$\%F = \frac{\text{Initial Weight - Final Weight}}{\text{Initial Weight}} \times 100 \quad (6)$$

Weight variation

20 tablets were chosen at random, and weighed on a digital scale. From the overall weight, the average of three weights was determined. Calculations were made of the percentage deviations from the mean [20].

$$\text{Weight variation} = \frac{W1 - W2}{W2} \times 100 \quad (7)$$

where, W1 is the initial weight of the tablet and W2 is the average weight of the tablet.

Disintegration test

Utilising a digital microprocessor-based disintegration test device, the disintegration time of tablets was ascertained. Each tube received one tablet, which also contained a disc. The assembly was submerged in a water-filled, 1000 mL beaker. The amount of water in the beaker was such that the wire mesh was at least 25 mm above and below the water's surface at its highest and lowest points, respectively. The equipment was run and kept at a temperature of 37°C. All tablets took the same amount of time to break up and travel through the wire mesh [20].

Dissolution test

The USP Dissolution Apparatus II was used to measure the Polyherbal chewable tablet's dissolution profile in 900 ml of water at 370.5°C and 100 rpm of stirring at 10, 20, 30, 40, 50 and 60 minutes. Various samples were taken out and replaced with simulated fluid of the same amount. Using Whatman filter paper, samples were subsequently filtered, and their absorbance was measured via a UV spectrophotometer and a calibration curve [20].

Statistical analysis

The results are presented as mean (±SD) and were analyzed by using the GraphPad Prism 5.0 (GraphPad Software, Inc., San Diego, CA, USA). A difference below the probability level of P-value = 0.05 was calculated using ANOVA [21].

***In-vitro* acid-neutralizing capacity assessment**

the acid-neutralizing capacity of the formulated tablets was evaluated using the pH meter method and the method stipulated in USP 29.

For the pH meter method, 60 mL of 0.1 N Hydrochloric Acid (HCl) was poured into a beaker, and the initial pH was measured and recorded using a pH meter. Three tablets from each batch were triturated using a mortar and pestle and then carefully introduced into the beaker containing the HCl.

The mixture of 0.1 N HCl and the antacid tablets was stirred for 10 minutes. The final pH of the mixture was then determined using the pH meter. Data was accordingly collected and noted [22]. For the USP 29 method, an acid-neutralizing capacity test was conducted at a temperature of 37°C. The pH meter was standardized by employing 0.05 M potassium biphthalate and 0.05 M potassium tetraoxalate standard buffers. A magnetic stirrer ensured consistent stirring at a rate of 300±30 rpm. Each formulation (1 gram) was placed in a 250 mL beaker, to which 70 mL of distilled water was added. This mixture was stirred for a minute using the magnetic stirrer. After the addition of 30 mL of 1.0 N HCl, the test solutions were stirred continuously for another 15 minutes. To achieve a consistent pH of 3.5, additional HCl was titrated with 0.5 N Sodium Hydroxide (NaOH) [23].

The total milliequivalents (mEq) of acid consumed was calculated using the formula:

$$\text{Total mEq} = 30 \times \text{NHCl}) - (\text{VNaOH} \times \text{NNaOH})$$

where, NHCl and NNaOH represent the normality of hydrochloric acid and sodium hydroxide, respectively, and VNaOH represents the volume of sodium hydroxide. The result was expressed in terms of total mEq per gram of substance [25-27].

RESULTS

Results of calibration curve of polyherbal extract

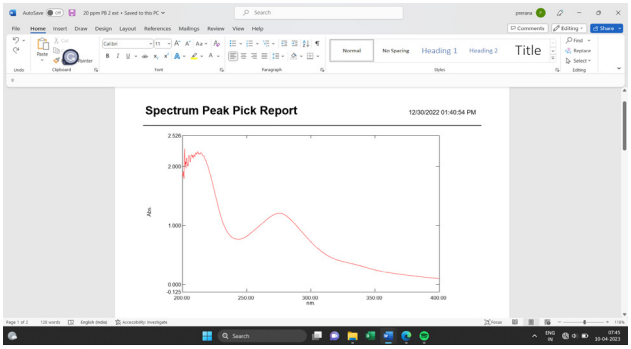

Figure 1. Maximum absorption wavelength of Polyherbal extracts at 275 nm

Table 2. Standard calibration curve concentrations and absorbances

Concentration (µg/ml)	Absorbance
5	0.044
10	0.072
15	0.097
20	0.119
25	0.145
30	0.169
Absorbance Maximum	275 nm
Slope	0.0051
Intercept	0.0184
Correlation Coefficient (r^2)	0.9972

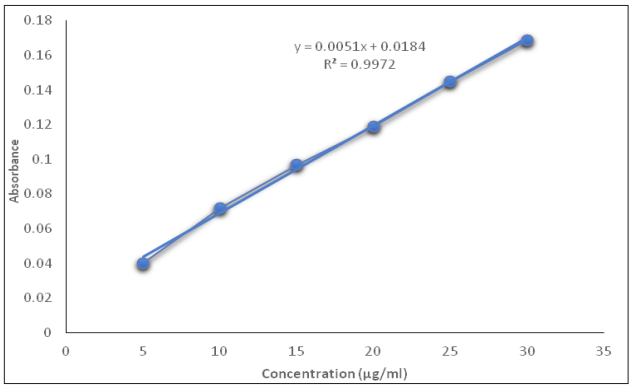

Figure 2. Standard calibration curve for polyherbal extracts

Results of drug - Excipient FTIR compatibility study

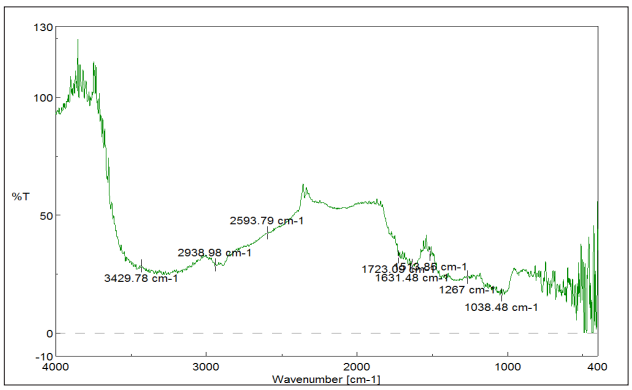

Figure 3. FT-IR spectra of *Phyllanthus emblica* and *Glycyrrhiza glabra* combination

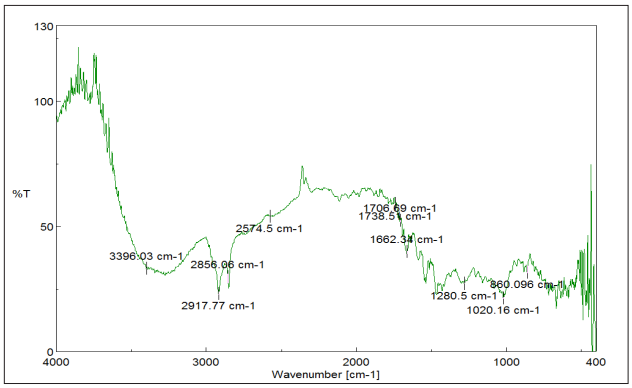

Figure 4. FTIR spectra of excipients

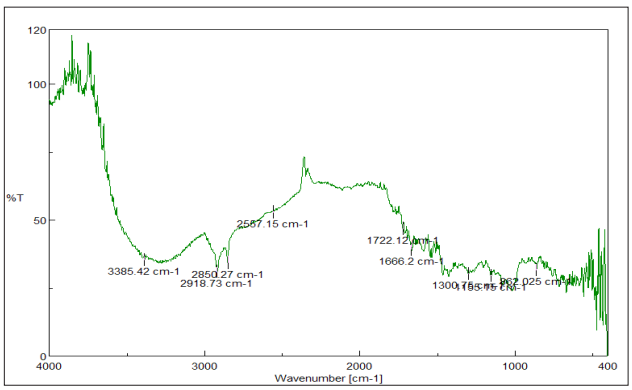

Figure 5. FT-IR spectra of combined the Pure drug + excipients

Evaluation of polyherbal tablets

Results of pre-compressional studies of powder blend

The prepared powder blend's bulk density, tapped density, compressibility index, Hausner'ss ratio and angle of repose were all analysed and the results shown in Table 3.

Table 3. Pre-compressional studies of powder blend

Batches	Bulk Density (g/ml)	Tapped Density (g/ml)	Carr's Index (%)	Hausner's ratio	Angle of repose (Θ)
PF1	0.438	0.541	19.03	1.23	34.9
PF2	0.442	0.557	20.64	1.26	35.21
PF3	0.423	0.524	19.27	1.23	34.28
PF4	0.421	0.557	24.41	1.32	33.7
PF5	0.418	0.507	17.55	1.21	33.98
PF6	0.425	0.509	16.50	1.19	34
PF7	0.431	0.503	14.31	1.16	34.59
PF8	0.420	0.543	22.65	1.29	34.89
PF9	0.400	0.496	19.35	1.24	33.68

Results of post-compression parameters

The results of Thickness, Hardness, Friability and weight variation of all batches are displayed in Table 4.

Table 4. Evaluation parameters of polyherbal tablets

Batches	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Weight variation	Disintegration time (Min)
PF1	4.87±0.04	4.9±0.1	0.76±0.3	404.8±0.2	17.4±0.54
PF2	4.84±0.02	6.1±0.9	0.3±0.2	405.2±0.8	7.4±0.24
PF3	4.86±0.01	5.7±0.2	0.63±0.2	405.6±1.1	10.1±0.35
PF4	4.85±0.02	5.5±0.3	0.7±0.4	402.7±0.5	9.3±0.65
PF5	4.9±0.01	5.3±0.1	0.42±0.7	399.4±0.8	19.9±0.34
PF6	4.87±0.04	5.2±0.1	0.71±0.9	404.1±0.7	12.8±0.23
PF7	4.88±0.06	5.1±0.1	0.64±0.2	403.2±0.6	16.5±0.74
PF8	4.89±0.02	5.7±0.1	0.74±0.2	404.8±0.8	15.6±0.87
PF9	4.88±0.03	5.8±0.2	0.5±0.2	402.2±0.9	5.6±0.98

Values are expressed in mean±SD (n=3)

Results of in-vitro drug release study

Table 5. *In-vitro* drug release study of formulations PF1 to PF9

Time (min)	PF1	PF2	PF3	PF4	PF5	PF6	PF7	PF8	PF9
0	0	0	0	0	0	0	0	0	0
10	12.27	18.13	16.58	12.85	9.6	16.8	10.52	20.91	22.58
20	22.01	33.01	28.76	24.07	12.04	25.36	14.69	34.72	35.26
30	35.99	48.63	41.23	39.47	26.1	34.32	30.96	49.43	50.72
40	46.91	57.55	53.94	49.52	33.74	43.33	38.59	60.82	67.32
50	62.43	67.92	68.93	66.25	44.07	57.69	49.13	76.72	81.06
60	68.42	80.7	79.33	64.68	50.27	72.03	60.23	88.13	98.63

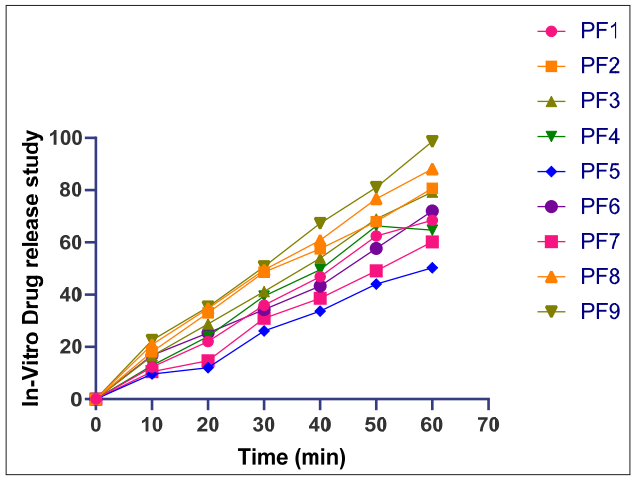

Figure 6. *In-vitro* drug release study of formulations PF1 to PF9

In-vitro acid neutralization capacity test of all batches with marketed formulation

Comparative Acid neutralization capacity of all batches with Marketed formulation results are shown in Table 6 and Figure 7.

Table 6. Comparative acid neutralization capacity of optimized batches with Standard formulation

Batches	The pH of Antacid – An acid mixture	ANC mEq/g
Phyllanthus emblica	6.87±0.23	21.35±0.53
Glycyrrhiza glabra	5.90±0.54	18.65±0.87
Combine extract	8.69±0.33	27.83±0.34
PF3	5.25±0.21	18.28±0.65
PF8	5.16±0.63	24.30±0.78
PF9	5.02±0.54	28.12±0.43
Marketed Formulation		
Gelusil	8.48±0.32	26.68±0.65
Qdee	4.06±0.11	21.82±0.45

Values are expressed in mean±SD (n=3)

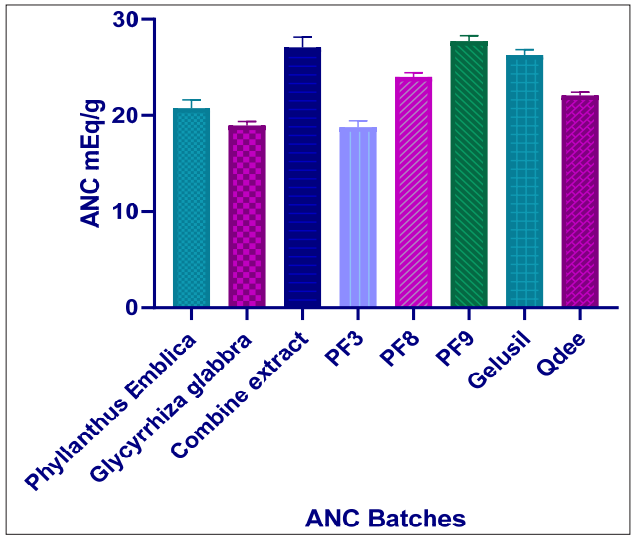

Figure 7. Comparative study of acid neutralization capacity of extracts, optimized batches and marketed formulation

DISCUSSION

The results of the standard calibration curve of the polyherbal extract offer valuable insight into the absorption characteristics and concentration-dependent response of the formulation. The maximum absorption wavelength of the polyherbal extracts was determined to be 275 nm (Figure 1). This wavelength is crucial as it allows for the quantification of the polyherbal extract in a mixture by taking advantage of the specific absorbance of the compounds at this wavelength.

Data presented in Table 2 highlights the absorbance values corresponding to varying concentrations of the Polyherbal extract, ranging from 5 to 30 µg/ml. It can be observed that as the concentration of the extract increases, there is a corresponding increase in absorbance. For instance, at a concentration of 5 µg/ml, the absorbance recorded was 0.044, which gradually increased to 0.169 at a concentration of 30 µg/ml. This positive correlation confirms the concentration-dependent response of the Polyherbal extract in solution [28].

The standard calibration curve (Figure 2) showcases this relationship between the concentration of the Polyherbal extract and the measured absorbance. The correlation coefficient (r^2) value obtained was 0.9972, indicating a strong linear relationship between concentration and absorbance, affirming the reliability of Beer-Lambert's law within this concentration range. The slope of 0.0051 and an intercept of 0.0184 further corroborates this strong linearity.

The FT-IR compatibility study between the Polyherbal extract, comprising *Phyllanthus emblica* and *Glycyrrhiza glabra*, and the selected excipients, serves as a vital assessment in the development of the chewable antacid tablet formulation [29]. It assists in ensuring that no significant chemical interactions occur between the herbal constituents and the excipients that might compromise the tablet's stability, efficacy or safety.

The FT-IR spectra of the *Phyllanthus emblica* and *Glycyrrhiza glabra* combination (Figure 3) shows characteristic peaks at various wavelengths, corresponding to different functional groups. The observed peaks align with the standard absorbance values for respective functional groups such as O-H stretch (3429.79 cm^{-1}), C=O (1723.09 cm^{-1}), C=C (1631.48 cm^{-1}), C-C (1038.48 cm^{-1}), COOH (2938.98 cm^{-1}), and C-O (1267 cm^{-1}).

The FT-IR spectra of the excipients (Figure 4) are also presented with significant peaks observed at wavelengths corresponding to the functional groups such as O-H (3396.03 cm^{-1}), Mg (2917.77 cm^{-1}), C-H (2856.66 cm^{-1}), H-Si-R (2574.5 cm^{-1}), C=O (acid) (1706.69 cm^{-1}), C=O (1738.51 cm^{-1}), C=C (1662.38 cm^{-1}), C-O (1280.5 cm^{-1}), C-C (1020.16 cm^{-1}), and C-H bend (860.096 cm^{-1}). Upon analyzing the FT-IR spectra of the combined pure drug and excipients (Figure 5), it is notable that the characteristic peaks remain largely consistent with those observed separately in the drug and excipient spectra. This consistency implies that no major chemical interactions occur between the herbal components and the excipients used in the formulation [30]. In conclusion, the FT-IR compatibility study results suggest that the *Phyllanthus emblica* and *Glycyrrhiza glabbra* extracts can be suitably combined with the chosen excipients for the formulation of the chewable antacid tablets, without encountering significant chemical interactions that may alter the tablet's performance. The absence of new or shifting peaks in the combined drug-excipient spectrum is indicative of the compatibility of these constituents in the designed formulation.

The pre-compressional studies of the powder blend provided valuable insights into the flowability and compressibility characteristics of the formulations, which are pivotal parameters in the direct compression process for tablet manufacturing. The powder blend's bulk density, tapped density, compressibility index (Carr's index), Hausner's ratio and angle of repose for different formulations were determined (Table 3).

The bulk and tapped densities ranged from 0.400 to 0.442 g/ml and 0.496 to 0.557 g/ml across the formulations, respectively. Both of these measures play a significant role in determining the blend's packing behaviour and directly influence the tablet's weight uniformity. The Carr's index, which gauges the powder's compressibility and its potential to form a good-quality tablet, ranged from 14.31% to 24.41% across all the batches. A Carr's index below 15% is considered excellent, while an index between 15% and 25% is indicative of satisfactory to passable flowability. In this regard, most batches seem to fall within the acceptable range, indicating acceptable compressibility [31-33]. The Hausner's ratio, another measure of flowability, varied between 1.16 and 1.32. A ratio less than 1.25 is indicative of good flowability, while a ratio between 1.25 and 1.5 suggests passable to poor flowability. As observed, most of the formulations showcase reasonable flowability, ensuring that the blend will flow uniformly into the die cavity during tablet compression. Lastly, the angle of repose was in the range of 33.68° to 35.21°. An angle of repose below 35° indicates good flowability. Hence, the results demonstrate that the formulations possess acceptable flow properties.

The post-compression evaluation of the Polyherbal tablets involved various critical parameters such as thickness, hardness, friability, weight variation and disintegration time (Table 4).

Thickness of the tablets, which is a crucial factor affecting the tablet's physical stability and patient compliance, ranged from 4.84 mm to 4.9 mm for all batches. The minimal variance in thickness within the batches implies a consistent die filling during the compression process. Hardness is an essential parameter as it influences the tablet's ability to withstand mechanical shocks during handling, packaging and transportation. The hardness of the tablets ranged from 4.9 kg/cm^2 to 6.1 kg/cm^2, indicating that the tablets are sturdy enough to resist breaking under normal conditions. Friability, a measure of tablet strength in the face of abrasion, was within the acceptable range (below 1%) for all formulations, suggesting a high degree of resistance to chipping or crumbling, which is crucial during packaging and transportation.

The uniformity of tablet weights within a batch is critical to assure the consistent dose of the active drug. The weight variation results complied with the standard limits, ensuring a uniform distribution of the active constituents in each tablet. Disintegration time is an important measure that can

affect the rate and extent of drug absorption. The disintegration time of tablets varied from 5.6 minutes to 19.9 minutes across the formulations [34]. The optimal disintegration time ensures that the tablet disintegrates and releases the active components once it reaches the stomach. In conclusion, the post-compression evaluation confirmed that the tablets were of sound quality and complied with the standard pharmacopoeial limits for various parameters, indicating a high degree of uniformity and consistency in the manufacturing process.

The *in-vitro* drug release study provides insights into the release behaviour of the active components from the Polyherbal tablets, which is crucial for their efficacy. The drug release profiles of the nine formulations (PF1 to PF9) are presented in Table 5 and are depicted in Figure 6. Observing the drug release at different time points, it is apparent that the release of active components varies across the formulations. After 60 minutes, PF9 exhibited the highest drug release rate at 98.63%, while PF5 showed the slowest release rate at 50.27%. The other formulations demonstrated intermediate release rates, with PF2 and PF8 showing promising release rates of 80.7% and 88.13%, respectively [35]. This variation in drug release rates could be attributed to differences in the formulation components, particularly the choice of excipients, which can significantly influence the dissolution behaviour of the tablets. The physical and chemical properties of the excipients, such as their solubility, hygroscopicity and interaction with the active components, might affect the release of the active constituents from the tablet matrix. The superior performance of PF9 might be attributed to an optimal combination of excipients, providing a balance between tablet integrity (preventing premature disintegration) and allowing sufficient permeability for the dissolution medium to ingress and dissolve the active components. In contrast, the lower drug release rate of PF5 may be due to the presence of certain excipients which could be creating a more tightly bound matrix, restricting the drug release. The variability in the drug release profiles among the formulations underscores the importance of carefully optimizing the formulation components so as to achieve the desired drug release rate.

The *in-vitro* acid neutralization capacity (ANC) test provides essential information on the efficacy of antacid formulations in neutralizing gastric acid, a key factor for reducing symptoms associated with conditions such as acid reflux and gastric ulcers. In this context, the ANC values for various batches of Polyherbal formulations were compared with standard marketed formulations, Gelusil and Qdee, as shown in Table 6 and Figure 7. Observing the data, it is clear that the acid neutralization capacities of the formulations vary. Among the individual extracts, the *Phyllanthus emblica* extract exhibited a higher ANC value (21.35±0.53 mEq/g) compared to the *Glycyrrhiza glabra* extract (18.65±0.87 mEq/g). The combined extract showed an even higher ANC value (27.83±0.34 mEq/g), indicating a synergistic effect in neutralizing acid when the two extracts are used together [36]. Among the formulated batches, PF9 exhibited the highest ANC value (28.12±0.43 mEq/g), closely followed by PF8 (24.30±0.78 mEq/g). These batches demonstrated higher ANC values than PF3 (18.28±0.65 mEq/g), indicating that the formulation process and the selection of excipients have substantial influence on the ANC [36]. Comparing with the standard marketed formulations, the ANC of PF9 was significantly higher than Gelusil (26.68±0.65 mEq/g) and Qdee (21.82±0.45 mEq/g), indicating that the Polyherbal formulation may offer a more effective means of acid neutralization. However, the pH of the antacid-acid mixture was found to be lower for the formulated batches compared to the combined extract and Gelusil. This suggests that while the formulated batches might neutralize more acid, the extracts and Gelusil may better maintain a higher pH in the presence of acid.

The findings from this study underscore the potential of the Polyherbal tablets in neutralizing gastric acid, with PF9 showing the most promising results. However, further *in-vivo* studies are needed to validate these *in-vitro* findings and assess the clinical efficacy and safety of these formulations. It's also crucial to note that while achieving high ANC values is important, the overall formulation should also take into consideration other factors such as patient compliance, cost-effectiveness and potential side effects.

CONCLUSION

In conclusion, the investigation into the development and characterization of Polyherbal tablets comprising *Phyllanthus emblica* and *Glycyrrhiza glabra* extracts demonstrated promising results. The study systematically assessed various aspects including calibration curve of the Polyherbal extract, drug-excipient FTIR compatibility, pre-compressional and post-compressional characteristics, *in-vitro* drug release and *in-vitro* acid neutralization capacity. The drug-excipient compatibility studies using FTIR confirmed that there was no significant interaction between the drug and the selected excipients. Pre-compressional studies revealed that the powder blend showed suitable flow properties, and post-compressional parameters demonstrated that the tablets complied with pharmacopeial specifications for thickness, hardness, friability, weight variation and disintegration time. The *in-vitro* drug release study of the Polyherbal tablets displayed a controlled and sustained release pattern. Most importantly, the *in-vitro* acid neutralization capacity tests showed that certain formulations, notably PF9, exhibited a higher acid neutralizing capacity than even the standard marketed formulations. This indicates the significant potential of these Polyherbal tablets as effective antacid agents. These findings suggest that Polyherbal tablets with *Phyllanthus emblica* and *Glycyrrhiza glabra* could offer a promising alternative to existing antacid formulations. However, further *in-vivo* studies and clinical trials will be essential to confirm the *in-vitro* results, ascertain the bioavailability of the active ingredients, and evaluate the safety and tolerability of these tablets. The positive results from this study encourage further research and development of these Polyherbal tablets as an effective therapeutic strategy for managing gastric acid-related disorders.

FUTURE SCOPE

The future scope of exploring the synergistic effect in Polyherbal chewable antacid tablets holds great potential for advancing the field of pharmaceutical research, improving therapeutic

outcomes, and meeting the growing demand for natural and personalized healthcare solutions.

ABBREVIATIONS

FTIR – Fourier-Transform Infrared Spectroscopy;
PF1-PF9 – Different Formulation Batches;
HCL – Hydrochloric Acid;
NaOH – Sodium Hydroxide;
mEq – Milliequivalent;
USP 29 – United States Pharmacopeia 29;
O-H – Hydroxyl Group;
C=O – Carbonyl Group;
C=C – Carbon-Carbon Double Bond;
C-C – Carbon-Carbon Single Bond;
COOH – Carboxyl Group;
C-O – Carbon-Oxygen Single Bond;
MG – Magnesium;
H-SI-R – Silane Group;
C=O (ACID) – Carboxylic Acid;
C-H – Carbon-Hydrogen Single Bond;
C-H bend – Bending Vibration of Carbon-Hydrogen Bond;
SD – Standard Deviation;
ANC – Acid Neutralization Capacity;
Ɵ – Angle;
r^2 – Coefficient of Determination.

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CONFLICT OF INTEREST

The author declared that there is no any conflict of interest in this study.

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REFERENCES

1. Sharma S, Sharma P, Katiyar D, Goel R, Sahoo J. Formulation, standardization and screening of polyherbal churna for antacid activity. *Int J Res Ayurveda Pharm*. 2018;9(4):94-7.
2. Ramana VK, R VK, Rsnakk C, Subhadra S, Professor A. Assessment of in vitro antacid activity of different root extracts of Tephrosia purpurea (L) pers by modified artificial stomach model. *Asian Pac J Trop Biomed*. 2012:2(3):1487-92.
3. https://nativecare.icliniq.com/articles/gastro-health/hyperacidity
4. Reddy AS, Reddy DRK, Prasad NAV. *Herbal and pharmaceutical drugs enhanced with probiotics*. United States Patent; 2000;44-87.
5. Parasuraman S, Thing GS, Dhanaraj SA. Polyherbal formulation: Concept of Ayurveda. *Pharmacogn Rev*. 2014;8:73-80.
6. Michele TM, Knorr B, Vadas EB, Reiss TF. Safety of chewable tablets for children. *Ann Pharmacother*. 2002;36(3):391-403.
7. Strickley RG, Iwata Q, Wu S, Dahl TC. Pediatric drugs – a review of commercially available oral formulations. *J Pharm Sci*. 2008;97(5):1731-74.
8. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. CBS Publishers & Distributors; 2009:182-303.
9. Kushwaha SK, Jain A, Jain A, Gupta VB, Patel JR. Hepatoprotective activity of the fruits of Momordica dioica. *Niger J Nat Prod Med*. 2005;9:29-31.
10. Singh E, Sharma S, Pareek A, Yadav S, Sharma S, Dwivedi J. Phytochemistry, traditional uses and cancer chemopreventive activity of Amla (*Phyllanthus emblica*): The sustainer. *J Appl Pharm Sci*. 2011; 2(01):176-83.
11. Khan KH. Role of Emblica officinalis in medicine-a review. *Bot Res Int*. 2009;2(4):218-28.
12. Jayaweera DMA. Medicinal plants (indigenous and exotic) used in Ceylon: Acanthaceae-Burseraceae. Colombo: National Science Council of Sri Lanka. 1980;4(2).
13. Talreja S, Kumari S, Srivastava P, Pandey S. A complete pharmacognostic review on amla. *World J Pharm Pharm Sci*. 2020;(4):622-37.
14. Ch SVK. Lycopene: *Advancement in functional food ingredients* (book chapter). 2nd ed. 2019:78.
15. Nesar A, Noorul H, Khalid M, Juber A, Mujahid M, Badruddin, et al. *Glycyrrhiza glabra*: traditional uses and pharmacological actions. *Adv J Pharm Life Sci Res*. 2016;4(2):23-32.
16. Damle M. *Glycyrrhiza glabra* (Liquorice) – a potent medicinal herb. *Int J Herb Med*. 2014;2(2):132-6.
17. Kaur R, Kaur H, Dhindsa AS. *Glycyrrhiza glabra*: A phytopharmacological review. *Int J Pharm Sci Res*. 2013;4(7):2470-7.
18. Tewari D, Mocan A, Parvanov ED, Sah AN, Nabavi SM, Huminiecki L, et al. Ethnopharmacological approaches for therapy of jaundice: Part II. Highly used plant species from Acanthaceae, Euphorbiaceae, Asteraceae, Combretaceae, and Fabaceae families. *Front Pharmacol*. 2017;8.
19. Khare C. *Encyclopedia of Indian Medicinal Plants*. New York: Springer; 2004:233-5.
20. *Indian Pharmacopoeia*. Indian Pharmacopoeial Commission, Ghaziabad: Government of India. Ministry of Health and Family Welfare; 2014:3174-6, 3282-84.
21. WHO. *Quality control methods for medicinal plant materials*. Geneva: World Health Organization; 1998.
22. Bunaciu AA, Aboul-Enein HY, Fleschin S. Application of Fourier transform infrared spectrophotometry in pharmaceutical drugs analysis. *Appl Spectrosc Rev*. 2010;45(3):206-19.
23. Mallik S, Kshirsagar MD, Saini V. Studies on physical/chemical compatibility between synthetic and herbal drugs with various pharmaceutical excipients. *Sch Res Libr*. 2011;3(5):173-8.
24. *United States Pharmacopoeia* (USP34 NF29). Rockville: The United States Pharmacopeial Convention;2011:140-1.
25. Verma PRP, Shrivastava A, Pathria A. In vitro evaluation of some ayurvedic antacids. *Anc Sci Life*. 1996; XVI(2):152-5
26. Sunilson AJ, Said RB, Anandarajagopal K, Gnana Kumari A, Vimala A, Khan A, et al. Formulation and evaluation of herbal capsules containing dried ethanol extract of Gnetum gnemon fruits. *Int J Pharm Pharm Res*. 2018;12(1):273-80.
27. Banik B, Sharma A, Nasrin A. Development and evaluation of carminative herbal chewable tablets based on turmeric, fennel seed, and mango ginger. *Asian Pac J Health Sci*. 2021;8(3):141-5.
28. Aulton ME, Taylor KMG. *Aulton's Pharmaceutics. Vol. 3*. Churchill Livingstone; 2007:176-8.
29. Balekundri A, Shahapuri A, Patil M. Poly-herbal tablet formulation by design expert tool and i*n vitro* anti-lipase activity. *Futur J Pharm Sci*. 2020;6(1).
30. Anonymous: Indian Pharmacopoeia. Government of India, Ministry of Health and Family Welfare. New Delhi: Controller of Publication; 2007.
31. Singla S, Kumari P, Rana R, Thakur R, Goyal S. Formulation and evaluation of polyherbal tablets for management of osteoporosis. *J Bio Innov*. 2022;11(2):320-33.
32. Sahoo HB, Asati AK, Toppo FA, Kori ML. Evaluation of polyherbal formulation for diuretic activity in albino rats. *Asian Pac J Trop Dis*. 2012;2(11):442-5.

33. *Indian Pharmacopoeia*. Indian Pharmacopoeia Commission, Ghaziabad: Government of India. Ministry of Health and Family Welfare; 2010:819-20.
34. Osei-Asare C, Owusu FWA, Entsie P, Annan AK. Formulation and *in vitro* evaluation of oral capsules from liquid herbal antimalarials marketed in Ghana. *J Trop Med*. 2021;1-9.
35. Alalor CA, Avbunudiogba JA, Builders FP, Okpara LO. Biological standardization of some polyherbal formulations for antacid activity. *East Afr Sch J Med Sci*. 2019;2(1):12-6.
36. Suvarna I, Kumari A, Jeenal P, Tejas P, Pramod I. Biological standardization of some polyherbal formulations for antacid activity. *Sch Res Libr*. 2014;6(1):83-6.