



IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203




Human Journals

Research Article


September 2020 Vol.:19, Issue:2

© All rights are reserved by RAJASHREE MASHRU et al.

Evolution of Marketed Antacid Formulations by Developed Modified Artificial Stomach Model



IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals



**RAHUL KHEMCHANDANI, YOGESH
RATANPARA, MANE YASHASHREE,
RAJASHREE MASHRU***

*Department of pharmacy, Faculty of pharmacy,
Kalabhavan, The Maharaja Sayajirao University of
Baroda, Vadodara 390001, Gujarat, India*

Submission: 25 August 2020
Accepted: 31 August 2020
Published: 30 September 2020



HUMAN JOURNALS

www.ijppr.humanjournals.com

Keywords: Developed modified artificial stomach model, antacid effect, neutralization effect, duration of consistent neutralization of artificial gastric acid, marketed antacid formulations

ABSTRACT

The objective of this research is to evaluate the antacid formulations by measuring their efficacy via neutralization effect and duration of consistent neutralization of artificial stomach Juice. Antacids are a class of medicines which is used for hyperacidity and they act by neutralizing the acid in the stomach. They contain ingredients such as aluminum, calcium, magnesium, or sodium bicarbonate which act as bases (alkalis) to neutralize stomach acid and increase pH in the stomach. Antacids are used to treat the symptoms of Gastro esophageal Reflux Disease (GERD also called acid reflux), heartburn, or indigestion (also called dyspepsia). We developed a new modified artificial stomach model that simulates the conditions of the Human stomach. This model is used to determine the pH change of artificial gastric juice after adding test solutions of various marketed antacid formulations and measure its antacid effect. By evaluating six formulations against water we found that formulation 4 has the highest antacid effect compared to other formulations and ordered off the antacid effect of various formulations found to be Formulation 4>Formulation 2>Formulation 1>Formulation 3>Formulation 6>Formulation 5>Water. From this experiment, we concluded that our newly developed modified artificial stomach model is successfully measured the antacid effect of various marketed antacid formulations and it can be further developed to use in different studies of dissolution profile, bioavailability, and drug-drug interactions.

INTRODUCTION

The human digestive system starts from the mouth, esophagus, and extended to the stomach, small and large intestines, rectum, and anus. After ingestion of food, it breaks down both chemically and mechanically during digestion and nutrients absorbed^[1]. (Figure 1)^[1]. In the recent 20 to 30 years several in vitro methods have been developed to simulate the physiological conditions (temperature, agitation, pH, enzyme and chemical composition, mechanical attributes) and the order of events that occur during digestion in the human gastrointestinal tract. Static methods (also called biochemical methods and fixed methods) are the common and easier techniques in this respect and having two or three digestion steps (oral, stomach, and intestinal) whose products remain largely static in a single static bioreactor. These methods mimic a limited number of attributes of physiological digestion and do not simulate the physical processes such as shearing, mixing, hydration, changes in conditions over time, or peristalsis.^[2] (Figure 2 and Figure 3).^[3]

Hydrochloric acid (HCl) is secreted by the stomach, but the pH of the stomach is not necessarily the same as the pH of the hydrochloric acid.

In the Fasting condition, gastric pH is between 1.5 and 2. After eating, the gastric pH rises temporary to pH 3-6., but it decreases in throughout digestion as gastric acid is secreted.^[4]

Chemical Composition of Gastric Juice

The fluid in the stomach is called gastric juice. It is complex mixtures of various chemicals including gastric acid and various digestive enzymes. The followings are the functions of various molecules of gastric juice:

- **Water**-Water does not affect the pH of the stomach, but its function provides enough liquidity to gastric contents such as food, enzymes, and acids so they can easily mix. Water also improves and aid in the function of various digestive enzymes.
- **Mucous** - Mucous (or mucus) is produced by cells of the mouth, throat, and stomach. It makes food to simple to go all through the gastrointestinal tract and provide protection from gastric acid to the lining of the gastric or stomach wall. Cells of the throat or neck also secrete bicarbonate ions which neutralize the stomach acid and maintain acid-base balance into the stomach.

- **Hydrochloric Acid** - This strong acid is secreted by the parietal cells of the gastric wall. It eliminates microbes and other potential pathogens present in food and it actuates the catalyst pepsinogen into pepsin, which digests secondary and tertiary proteins into smaller, easily digested molecules-polypeptides.
- **Pepsinogen** - Pepsinogen is secreted by the stomach wall. It requires hydrochloric acid or low pH to digest protein.
- **Hormones and Electrolytes** - Gastric juice likewise contains hormones and electrolytes which are useful in organ work, supplement ingestion, and food absorption. Hormones are emitted by enteroendocrine cells.
- **Gastric Lipase** –It is secreted by stomach cells and which capacity helps in the absorption of fats.
- **Intrinsic Factor** - The parietal cells of the stomach secrete intrinsic factor, which is obligatory for vitamin B-12 absorption.
- **Amylase** –Generally this enzyme found in the stomach because of ingestion or gulping of salivation as it is available in spit and deactivated by Gastric acid. Again it secreted into a small intestine for digestion of carbohydrates. [4]

The mechanical stirring activity of the stomach combines all substance of the stomach to shape "chyme". After the stomach, chyme leaves the stomach and enters into the small intestine where basic enzymes neutralize the acidic chyme and further assimilation continues to absorb nutrients. [4]

Until now there is no specific description of the size or shape or structure of the human stomach. The human stomach is diverse in people and it is likewise relied upon on a huge number of biological factors. A normal physiological structure of the stomach seems to be like "J" shaped, hollow and flexible organ having approx more than 1 Litre capacity (Figure 4a) [5]. Based on these facts, a less complex 3-D model, capable of representing the average dimension of a human stomach in the postprandial period is demonstrated [5], [7]. As shown in Figure 4b [6], the model represents the stomach as a "J"-a shaped organ with a greater curvature of 32 ± 2 cm, a maximum transverse width of 9.5 ± 0.5 cm, a pylorus sphincter diameter of 1 ± 0.1 cm, and a capacity of 0.92 ± 0.2 L. [5], [7]

Resting stomach volume at the fasted state is as low as 25 ml. After ingestion of food, stomach expansion occurs and it is mainly proportional to stomach acid volume. The stomach secretes two to three liters of gastric juice every day. Instantly after food ingestion, the rate of secretion may rise from 1 ml/min under fasted conditions to 10 to 50 ml/min. The pH of the chyme varies between pH 6–7.^{[8], [9]} Mucus forms coagulated covering over the mucosal surface. Gastric juice contains 800-1000 µg/ml pepsin and about 1500µg/ml mucin.^{[10], [11]}

Hyperacidity also called acid dyspepsia is caused by excessive secretion of gastric acid in the stomach. It has symptoms include burning and pain in the chest and stomach, vomiting, loss of appetite, flatulence, and heartburn. On the off chance that this condition stays untreated for a long time, at that point it causes different complexities like gastric ulcers, chronic indigestion, and upper abdomen pain during muscular contractions, bloating, or gas and weight gain. Hyperacidity is generally caused by several external factors like eating habits, anxiety, and stress, smoking and alcohol consumption, lack of physical activity, and irregularity in eating patterns or disturbing natural biological cycles. It is a secondary condition to prolonged usage of certain medications like nonsteroidal anti-inflammatory drugs also predispose individuals to gastric acidity. Other predisposing factors for hyperacidity include bacterial infections generally by *Helicobacter pylori*, pregnancy, obesity, aging, and fasting.^[12] Hyperacidity problems can interfere with daily activities and cause anxiety and mood problems and ultimately person became less functional so this condition should be treated as soon as possible.^[13]

The currently used drugs for the treatment of hyperacidity include antacids (inorganic salts like aluminum hydroxide and magnesium trisilicate) which neutralize gastric acid, H₂ receptor antagonists which diminish gastric acid secretion for a prolonged duration (ranitidine, famotidine, nizatidine), proton pump inhibitors (omeprazole, lansoprazole, esomeprazole), tissue-lining protecting agents (sucralfate and misoprostol) and antibiotics (amoxicillin, metronidazole) for hyperacidity caused due to *Helicobacter pylori* infection.^[13]

This developed model is used for assessing the antacid efficacy by measuring the neutralization effect and the duration of consistent neutralization of artificial gastric acid.

MATERIALS AND METHODS

Chemicals and reagents:

Pepsin (From porcine gastric mucosa), sodium chloride, distilled water, 0.1 N Hydrochloric acid. All chemicals were obtained from local sources and were of analytical grade.

Following marketed formulations which were purchased from local pharmacy store:

1. Formulation 1 (Tablet containing: Dried Aluminium Hydroxide gel-300 mg + Magnesium Hydroxide-300 mg + Simethicone-25 mg)
2. Formulation 2 (Tablet containing: Dried Aluminium Hydroxide gel-300 mg + Magnesium Hydroxide-25 mg + Magnesium Aluminium Silicate Hydrate-50 mg + Activated Polydimethylsiloxane-25 mg)
3. Formulation 3 (Tablet containing: Dried Aluminium Hydroxide gel-250 mg + Magnesium Hydroxide-250 mg + Simethicone-50 mg)
4. Formulation 4 (Syrup containing: Dried Aluminium Hydroxide gel-415 mg + Magnesium Hydroxide-92.5 mg + Sodium Carboxy Methyl Cellulose-50 mg + Activated Polydimethylsiloxane-25 mg/5 ml)
5. Formulation 5 [Capsule containing: Mentha Oil (*Menthapiperetta* aerial part oil)-0.174 ml + Spearmint Oil (*Menthaspicata* aerial part oil)-0.034ml]
6. Formulation 6 (Powder containing: Sodium Bicarbonate-232 mg + Citric acid-218 mg + Sodium Carbonate-50 mg)

Material:

IV bag of 1000 ml, tubing, drip chamber, flow controller roller clamp, needle.

Instruments:

Instruments used in the study consisted of a standard pH meter, a magnetic stirrer with hot plate temperature controller, an adjustable electrode stand.

Design of Developed Modified Artificial Stomach Model:

Apparatus of Developed Modified Artificial Stomach Model (Figure 5a and Figure 5b) was made up of three elements:

pH recording system(R), Stomach(S), and Magnetic stirrer with a hot plate(M). The stomach was made up of three parts: Artificial gastric acid reservoir(S₁), Stomach chamber(S₂), and Discharge chamber(S₃). The reaction mixture was maintained at 37°C and stirred continuously at 30 rpm with a 2.5 cm magnetic stirring apparatus. Artificial gastric acid was pumped at 3 ml/min into S₂ through S₁, the inlet, and pumped out at 3 ml/min in S₃ through S₂, the outlet at the same time using flow regulators. A pH meter was connected to continuously monitor the changes in pH taking place in S₁.

Preparation of artificial gastric acid:

Sodium chloride (2 g) and pepsin (3.2 mg, 3200-4500 U/mg protein) were dissolved in 500 ml distilled water. Concentrated Hydrochloric acid (7 ml) and adequate distilled water were added to make a 1,000 ml solution. The pH of the solution was adjusted to 1.2 ^[14].

Preparation of test solution:

A test solution of Formulation 1, 2, 3 was prepared by the following method:

Take one tablet and crush it to form a powder and then add it to 100 ml distilled water.

A test solution of Formulation 4 was prepared by taking 5 ml of syrup and then added it to 100 ml of distilled water.

A test solution of Formulation 5 was prepared by taking one capsule and then placed it into 50 ml of distilled water and remained for 30 minutes then added it to 50 ml of distilled water and mixed it properly.

A test solution of Formulation 6 was prepared by taking 500 mg of powder and transferred it to 100 ml of distilled water.

Determination of pH:

The pH of the test solutions of Formulation 1, 2,3,4,5, and 6 was determined at a temperature of 37°C.

Determination of neutralizing effect on artificial gastric acid:^[14]

Test solutions of all Formulations (1, 2, 3, 4, 5, and 6) were added to the stomach chamber containing 100 ml of artificial gastric acid. The pH of each solution was determined at 37°C to examine the neutralizing effect on artificial gastric acid. A total of 7 experiments were performed separately with including water (procedure for water is the same as above).

Determination of the duration of consistent neutralization on artificial gastric acid in the developed modified artificial stomach model:^[15]

Each of test solution (100 ml) was added to S₂ (Stomach chamber) containing 100 ml of artificial gastric acid and Magnetic stirrer with a hot plate turned on for proper mixing of contents and temperature was maintained at 37 °C, after that artificial gastric acid was pumped at 3 ml/min into S₂ through S₁, the inlet and pumped out at 3 ml/min in S₃ through S₂, the outlet at the same time using flow regulators. A pH meter was connected to continuously monitor the changes in pH taking place in S₁. When the pH value returned to its initial value of 1.2, the duration of the neutralization effect was determined. Seven experiments were performed for each test solution viz. all Formulations (1, 2,3,4,5, and 6) and water.

Statistical analysis:

The experimental data obtained were expressed as mean \pm SEM, where SEM=Standard error of Mean; Comparison between the groups was analyzed by One-way Analysis of Variance(ANOVA). The differences were considered to be statistically significant when $**P<0.01$ where $n=6$.

RESULTS:

Neutralizing effect on artificial gastric acid:

The pH values of all test solutions and water were measured and then all six formulations pH value was compared with the pH of water. All formulations found to be having a higher neutralization effect on artificial gastric acid than water. (Table 1)

Duration of consistent neutralization on artificial gastric acid in the developed modified artificial stomach model:

The duration of consistent neutralization on artificial gastric acid of all test solutions found to be higher than the water. Amongst all test solutions, Formulation 4 has the highest antacid effect. The order of the antacid effect was as follows: Formulation 4>Formulation 2>Formulation 1>Formulation 3>Formulation 6>Formulation 5>Water. (Table 2) (All test solutions and water's antacid effect is shown in Figure 6, Figure 7, Figure 8, Figure 9, Figure 10, Figure 11, and Figure 12).

DISCUSSION AND CONCLUSION:

The Stomach is an organ that performs functions like propagation of food, mixing, and secretion of various enzymes with food, and absorption of nutrients. Approximately 2500 ml of Gastric acid juice is secreted by parietal cells of the stomach wall daily. Many Numerous microorganisms are executed by the acid of gastric juice and this acid also provides a low pH for protein digestion by pepsin enzyme. Mucosal erosion and ulceration occurred when aggressive factors such as gastric acid and pepsin cause damage to the defensive mechanism of gastric mucosa^[16].

The gastric mucosal defense mechanism is generally made up of the following parts according to the site of their location (Table 3)^[17].

Pre epithelial protection:

The main line of protection against aggressive factors is the mucus-bicarbonate barrier. The mucus cells of the gastric epithelium layer produce viscous gel and limited quantities of bicarbonate particles that keep up the epithelial cell surface at close to near-neutral pH^[17].

Epithelial protection:

The apical cell membrane has characteristic obstruction for gastric acid. A surfactants molecule of gastric epithelium such as amphoteric phospholipids increases the hydrophobicity of the biological membrane and prevents water-soluble agents in the gastric lumen from reaching and harming the gastric epithelial cell layer.

The Non-protein sulphydryl mixes are available in high amounts in the gastric epithelium layer which gives insurance against free radicals.

Human isthmus-pit cells have a division rate of 1/36 h and these cells differentiate into mucus cells from 48 to 96 hours.

Within an hour of damage, the process of restitution takes place. In which the superficial layer of the mucosa is nearly completely repaired with mucus cells which are derived from the gastric pits.^[17]

Subepithelial protection:

Removal of hydrogen ions and noxious agents generally took place by mucosal bloodstreams. The vascular arrangement at the subepithelial layer of gastric mucosa provides a unidirectional blood flow in mucosal exchange vessels and maintains an adequate balance of acid-base.

When damage occurred to this gastric mucosal defensive mechanism it causes different gastric issues like gastritis, peptic ulcer, and gastroesophageal reflux issue (GERD).

These conditions are generally treated by antacids, H₂ receptor antagonists, and proton pump inhibitors. Amongst them, antacids are used to utilize to treat ulcers. Antacids are inorganic salts that act by releasing anions into gastric juice and neutralize the acid of gastric juice by binding it and finally increases the pH of the stomach and provides alleviation against hyperacidity. These medications also increase intra-esophageal pH of the gastric lumen which finally causes a decline in pepsin activity^[17].

In the present study, we develop the modified artificial stomach model which mimicking the anatomy and physiology of the human stomach. We modify and make a simpler model of Avatier's artificial stomach model. In our modified model the natural anatomy of the stomach is preserved. We study the effect of antacids and compare their results statistically.

Developed modified stomach model made up of (as shown above in Figure 5) three chambers S₁, S₂, and S₃. This S₁ is a reservoir of artificial gastric juice that secretes artificial gastric juice into S₂ (stomach chamber) with a rate of 3 ml/min which is approximately the same as the natural human stomach's acid secretion rate. S₂ mimics the condition of the human stomach as peristalsis is mimicked by 30 rpm of magnetic stirrer with a hot plate which also maintains the temperature at 37 °C. S₃ is the discharge chamber and acts as a duodenum. This model allows the measurement of pH change occurred in the stomach chamber containing antacid formulation after the secretion of artificial gastric juice at steady-state i.e. 3 ml/min rate of

secretion. So we can measure the resistance induced by drug against acidification, which is proportional to the therapeutic effect of antacids. The more time is taken by test solution to come back at an initial pH of 1.2, the more potent an antacid formulation itself. Additionally, all test formulations are increased by pH of the stomach chamber and having significantly longer lag time for initial pH recovery i.e. pH of 1.2 compared to water indicating better and consistent antacid effects.

The highest potency or neutralization effect is seen in Formulation 4 due to the high amount of inorganic salts and it has the highest duration of consistent neutralization of artificial gastric juice. Further following order is seen in neutralizing the artificial gastric juice: Formulation 4>Formulation 2>Formulation 1>Formulation 3>Formulation 6>Formulation 5>Water.

From this, we also conclude that antifatulent drug-like simethicone as a negligible antacid or neutralizing effect. It may conclude that Formulation 4 having the highest concentration of dried aluminum hydroxide and a moderate amount of Sodium carboxymethyl cellulose i.e. viscosity enhancer has the highest neutralization effect and duration of consistent neutralization on artificial gastric acid.

This model is also used for the study of medicinal plants having antacid activity and also study the antacid effect of some common foods.

Extended application and further development of the model:

Application of this model can be enhanced by the addition of a Duodenum compartment, by adding duodenum compartment following application emerged as follows:

1. To study the dissolution profile of various drugs.
2. To study the relative bioavailability of various drugs.
3. To study the interaction of antacids with H₂ receptor antagonists.

Conflict of interest statement:

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS:

The authors express their deep sense of gratitude towards The Maharaja Sayajirao University of Baroda, Vadodara, Gujarat for providing necessary support, resources, and encouragement in the conducting research work.

REFERENCES:

1. Neil H. Mermelstein. Simulating Digestion. *Institute of Food Technologists(IFT)*. https://www.ift.org/news-andpublications/food-technology_magazine/issues/2010/december/columns/food-safety-and-quality. Published December 1, 2010. Accessed May 20, 2020.
2. Elisabet Fernández-García, Irene Carvajal-Lérida, Antonio Pérez-Gálvez. In vitro bioaccessibility assessment as a prediction tool of nutritional efficiency. *Nutrition Research. ELSEVIER*. 2009;29(11):751-760. doi:10.1016/j.nutres.2009.09.016
3. Kitty Verhoeckx, Paul Cotter, Iván López-Expósito. *The Impact of Food Bio-Actives on Gut Health*, 1st ed.; Charlotte Kleiveland, Tor Lea, Alan Mackie, Teresa Requena, Dominika Swiatecka, Harry Wichers, Eds.; In Vitro and Ex Vivo Models; Springer International Publishing: Switzerland, AG, 2015: 10-15.
4. Helmenstine Anne Marie, Ph.D. What Is the pH of the Stomach? *ThoughtCo*. <https://www.thoughtco.com/ph-of-the-stomach-608195>. Published February 21, 2020. Accessed May 20, 2020.
5. Maria J. Ferrua; R. Paul Singh. Modeling the Fluid Dynamics in a Human Stomach to Gain Insight of Food Digestion. *Journal of Food Science* **2010**, 75 (7), R151–R161. <https://doi.org/10.1111/j.1750-3841.2010.01748.x>.
6. Maria J. Ferrua; R. Paul Singh. Understanding the Fluid Dynamics of Gastric Digestion Using Computational Modeling. *Procedia food science*. 11th International Congress on Engineering and Food ICEF11. *ELSEVIER* **2011**, 1 (2011), 1465 – 1472. <https://doi.org/10.1016/j.profoo.2011.09.217>.
7. Schulze, K. (2006), Imaging and modelling of digestion in the stomach and the duodenum. *Neurogastroenterology & Motility*, 18: 172-183. doi:10.1111/j.1365-2982.2006.00759.x
8. CHM Versantvoort; E van de Kamp; CJM Rempelberg. *Development and Applicability of an in Vitro Digestion Model in Assessing the Bioaccessibility of Contaminants from Food*; RIVM report 320102002/2004; RIVM: National Institute for Public Health and the Environment, Bilthoven, the Netherlands, 2004; pp 9–32. Accessed May 20, 2020. <https://www.rivm.nl/en>.
9. Carolien H.M. Versantvoort, Agnes G. Oomen, Erwin Van de Kamp, Cathy J.M. Rempelberg, Adriënnne, J.A.M. Sips. Applicability of an in Vitro Digestion Model in Assessing the Bioaccessibility of Mycotoxins from Food. *Food and Chemical Toxicology. ELSEVIER* **2004**, 43 (1), 31–40. <https://doi.org/10.1016/j.fct.2004.08.007>.
10. Maria Vertzoni, Jennifer Dressman, James Butler, John Hempenstall, Christos Reppas. Simulation of Fasting Gastric Conditions and Its Importance for the in Vivo Dissolution of Lipophilic Compounds. *European Journal of Pharmaceutics and Biopharmaceutics. ELSEVIER* **2005**, 60 (3), 413–417. <https://doi.org/doi:10.1016/j.ejpb.2005.03.002>.
11. John R. Dean, Renli Ma. Approaches to Assess the Oral Bioaccessibility of Persistent Organic Pollutants: A Critical Review. *Chemosphere. ELSEVIER* **2007**, 68 (8), 1399–1407. <https://doi.org/doi:10.1016/j.chemosphere.2007.03.054>.
12. Tack J, Caenepeel P, Arts J, Lee K-J, Sifrim D, Janssens J. Prevalence of acid reflux in functional dyspepsia and its association with symptom profile: *Gut* 2005; 54: 1370-1376 <http://dx.doi.org/10.1136/gut.2004.053355>
13. John L Wallace. Recent Advances in Gastric Ulcer Therapeutics. *ELSEVIER* **2005**, 5 (6), 573–577. <https://doi.org/doi:10.1016/j.coph.2005.06.004>.
14. Vandana Panda, Priyanka Shinde, Jyoti Deora, Sanju; Gupta. A Comparative Study of the Antacid Effect of Some Commonly Consumed Foods for Hyperacidity in an Artificial Stomach Model. *Complementary Therapies in Medicine. ELSEVIER* **2017**, 34 (October 2017), 111–115. <https://doi.org/crossmark-logo> <https://doi.org/10.1016/j.ctim.2017.08.002>.

15. VATIER, J., MALIKOVA-SEKERA, E., VITRE, M.T. and MIGNON, M. (1992), an artificial stomach-duodenum model for the in-vitro evaluation of antacids. *Alimentary Pharmacology & Therapeutics*, 6: 447-458. doi:10.1111/j.1365-2036.1992.tb00558.x
16. Sandhya S, Venkata Ramana K, Vinod K R, Chaitanya Rsnakk. Assessment of in Vitro Antacid Activity of Different Root Extracts of Tephrosia Purpurea (L) Pers by Modified Artificial Stomach Model. *Asian Pacific Journal of Tropical Biomedicine. ELSEVIER* **2013**, 2 (3), S1487–S1492. [https://doi.org/10.1016/S2221-1691\(12\)60442-0](https://doi.org/10.1016/S2221-1691(12)60442-0).
17. Forssell, H., Gastric Mucosal Defence Mechanisms: A Brief Review. *Scandinavian Journal of Gastroenterology* **1988**, 23 (sup155), 23–28. <https://doi.org/10.3109/00365528809096277>.

Table No. 1: Neutralizing effect of water, Formulation 1, 2,3,4,5 and 6.

Formulation/sample	pH
Water	1.442 ± 0.003
Formulation 1	1.575 ± 0.002
Formulation 2	1.605 ± 0.002
Formulation 3	1.545 ± 0.003
Formulation 4	1.653 ± 0.003
Formulation 5	1.487 ± 0.002
Formulation 6	1.557 ± 0.002

Data are presented as mean ± SEM (n=6). P<0.001 when compared with water.

***SEM= the standard error of the mean**

Table No. 2: Duration of consistent neutralization in developed modified artificial stomach model of water, Formulation 1, 2,3,4,5 and 6.

Formulation/sample	Time(minutes)
Water	60.93 ± 0.034
Formulation 1	144.86 ± 0.067
Formulation 2	149.561 ± 0.044
Formulation 3	134.37 ± 0.091
Formulation 4	163.69 ± 0.087
Formulation 5	104.04 ± 0.183
Formulation 6	129.39 ± 0.068

Data are presented as mean ± SEM (n=6). P<0.001 when compared with water.

***SEM= the standard error of the mean**

Table No. 3: Gastric mucosal defense mechanism

1. Pre epithelial protection
<ul style="list-style-type: none"> • Mucus gel • Bicarbonate secretion
2. Epithelial protection
<ul style="list-style-type: none"> • Hydrophobicity of luminal cell membranes • Sulphydryl compounds • Rapid cell turnover • Restitution
3. sub epithelial protection
<ul style="list-style-type: none"> • Blood flow • Tissue acid-base balance

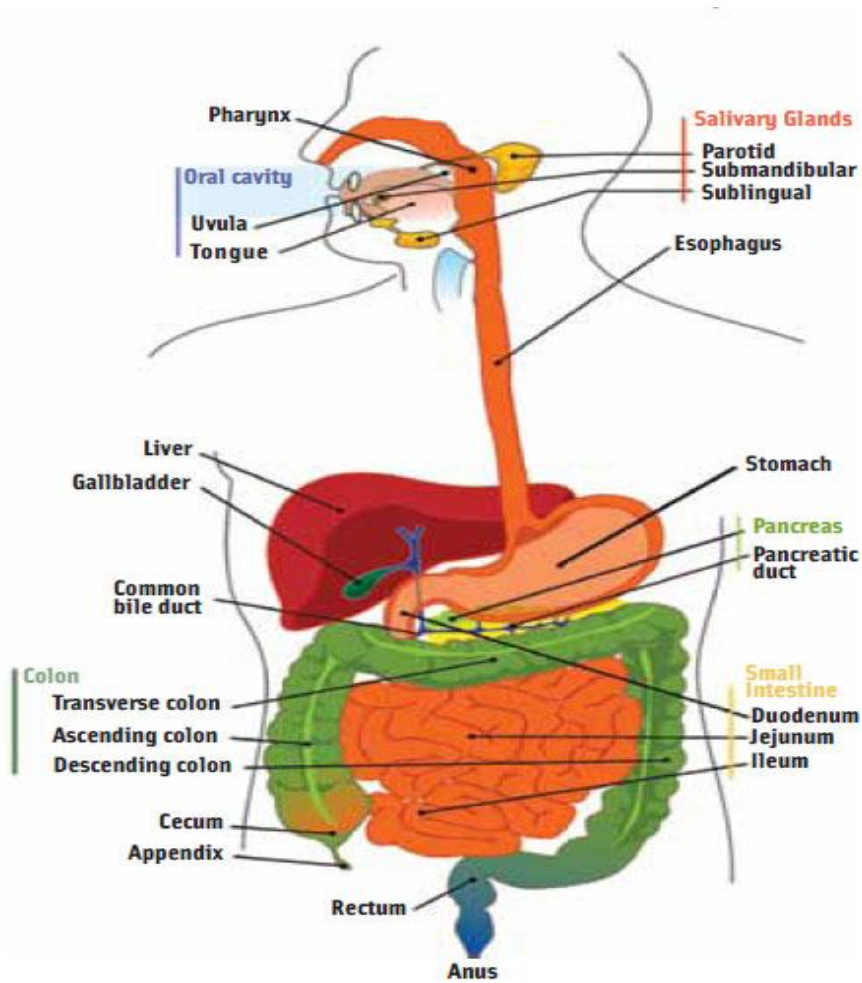


Figure No. 1: A schematic diagram of human digestive system or gastrointestinal tract

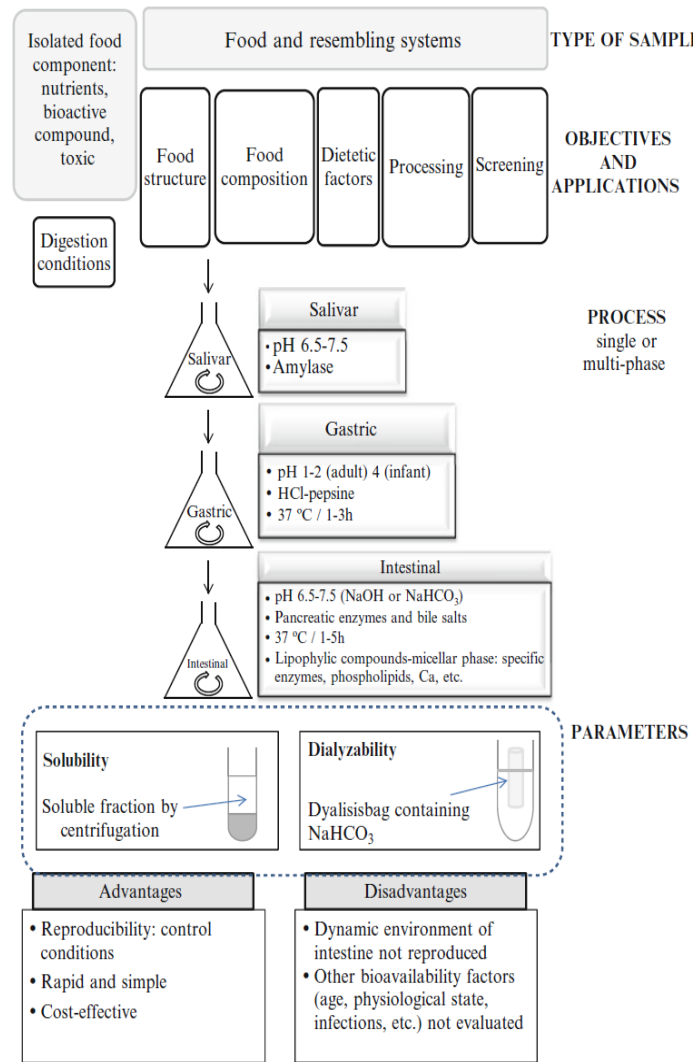


Figure No. 2: Overview on static model conditions

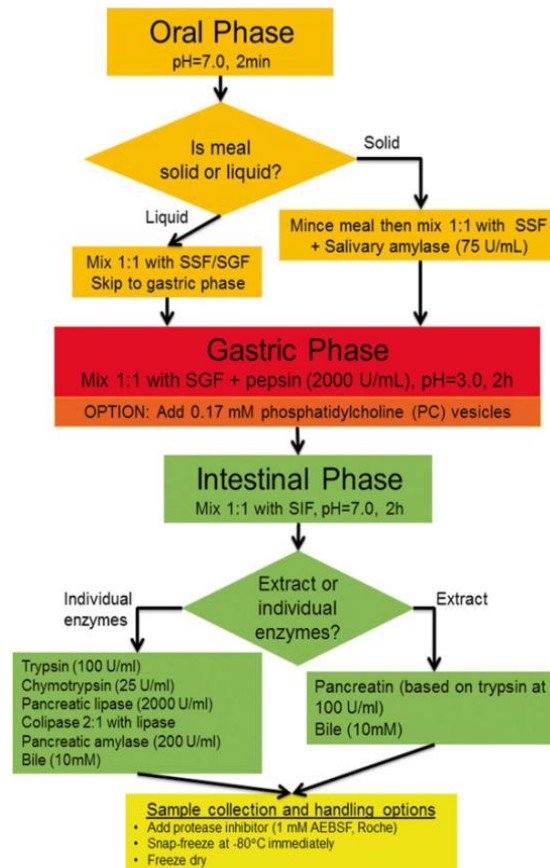


Figure No. 3: A flow diagram describing the InfoGest digestion method involving simulated salivary fluid(SSF), simulated gastric fluid (SGF) and simulated intestinal fluid (SIF)

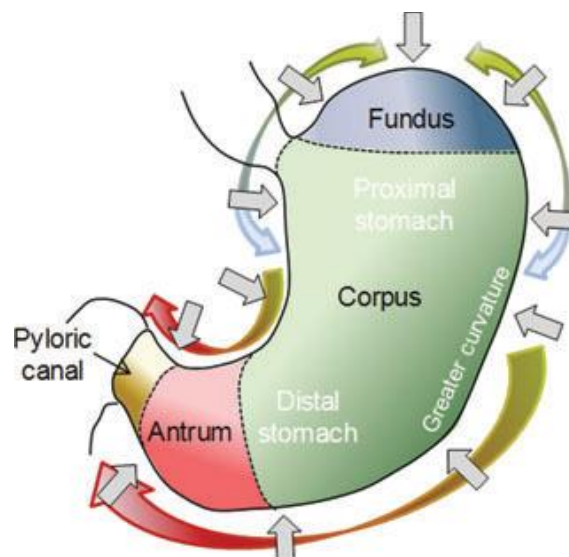


Figure No. 4a: A schematic diagram of human stomach

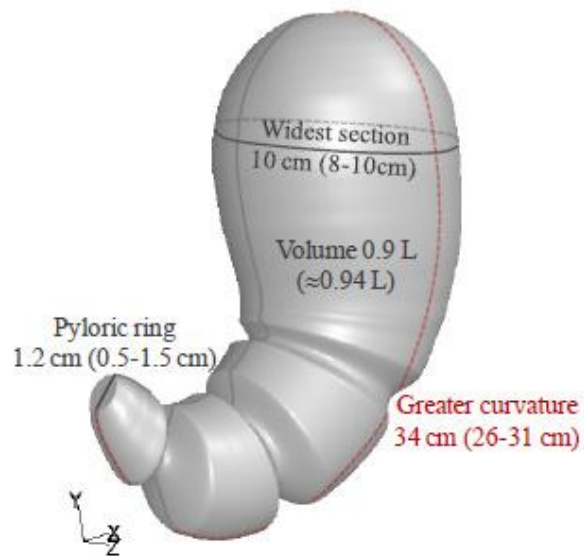


Figure No. 4b: Three-dimensional model of an average human stomach.

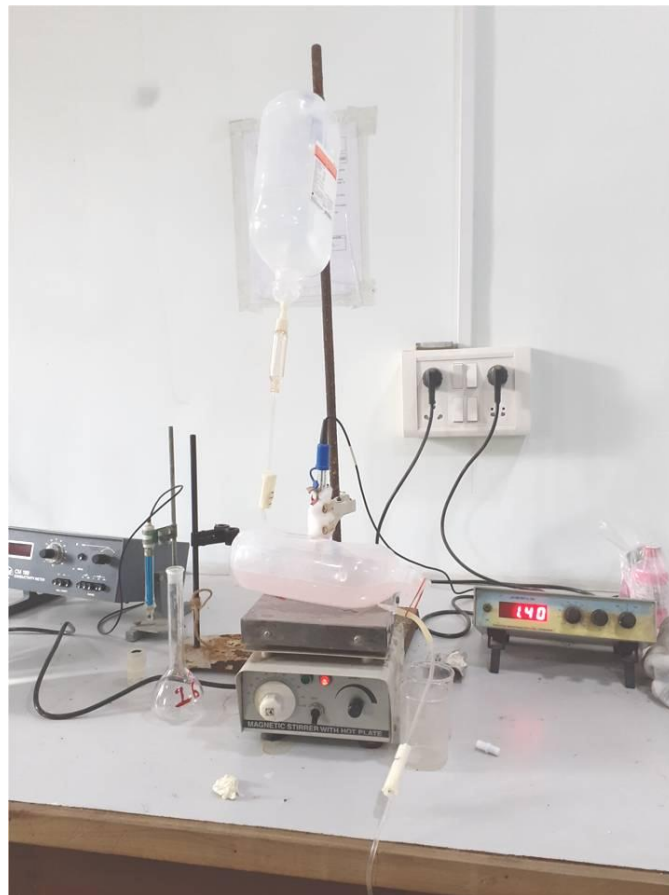


Figure No. 5a: Developed modified artificial stomach model

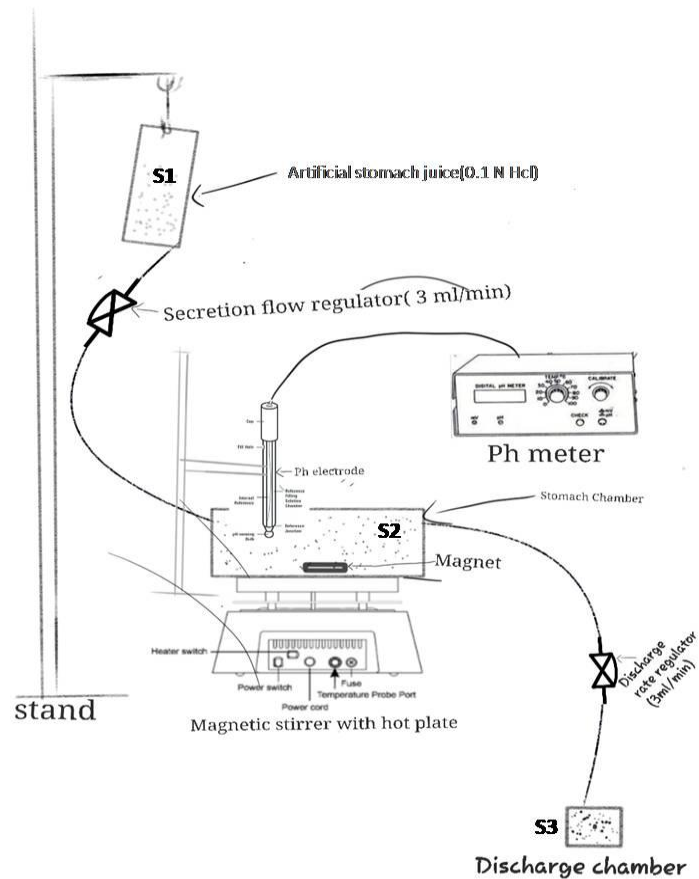


Figure No. 5b: Schematic representation of developed modified artificial stomach model

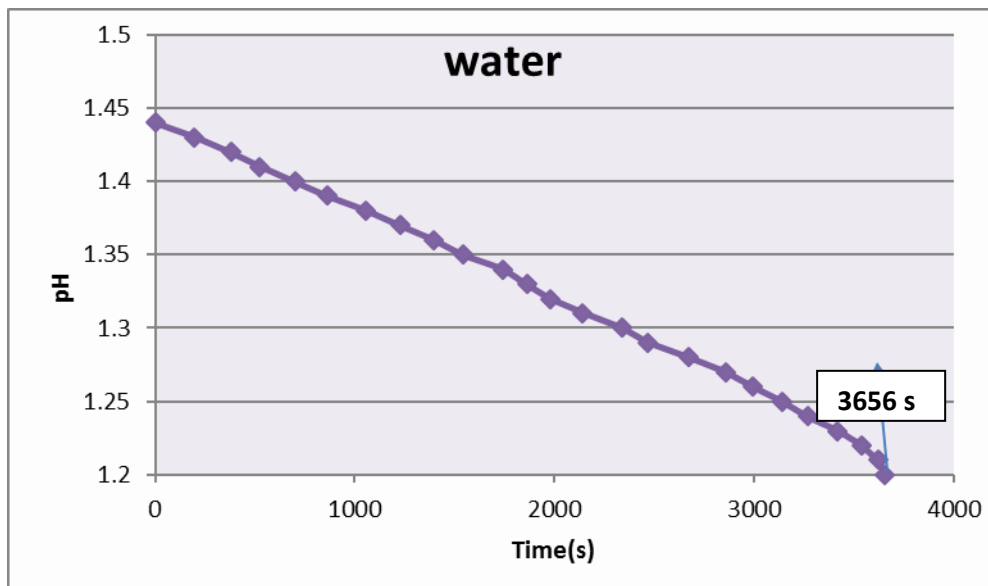


Figure No. 6: Duration of consistent neutralization of artificial gastric acid by water

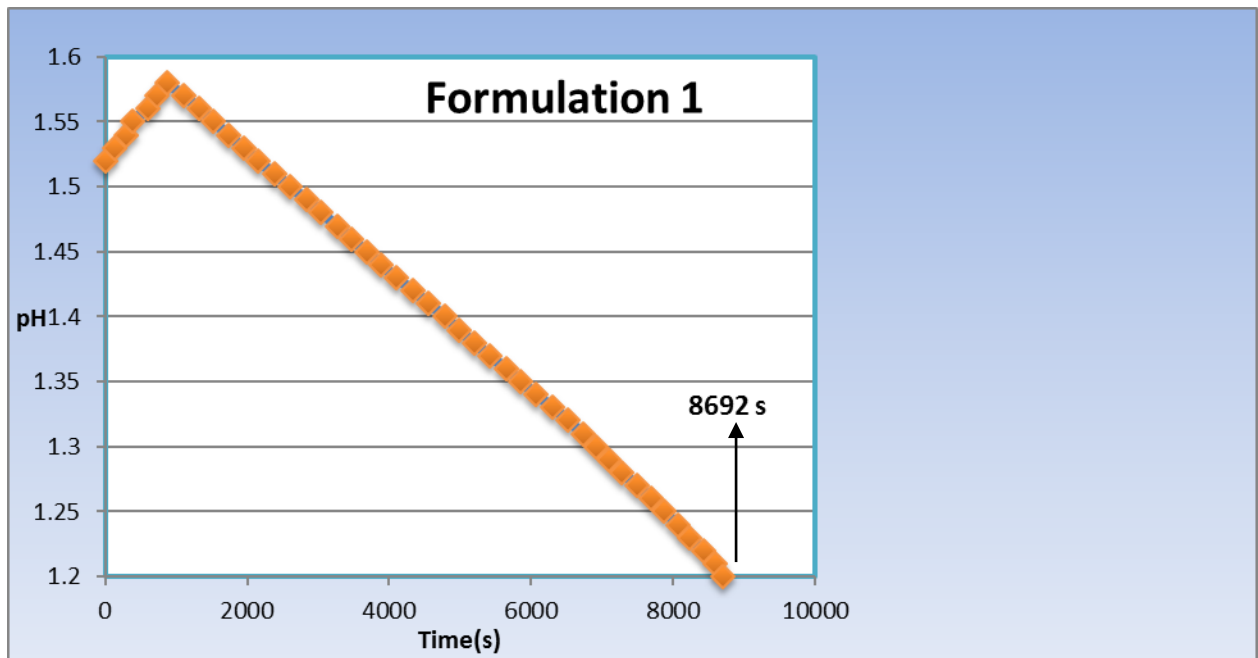


Figure No. 7: Duration of consistent neutralization of artificial gastric acid by Formulation 1

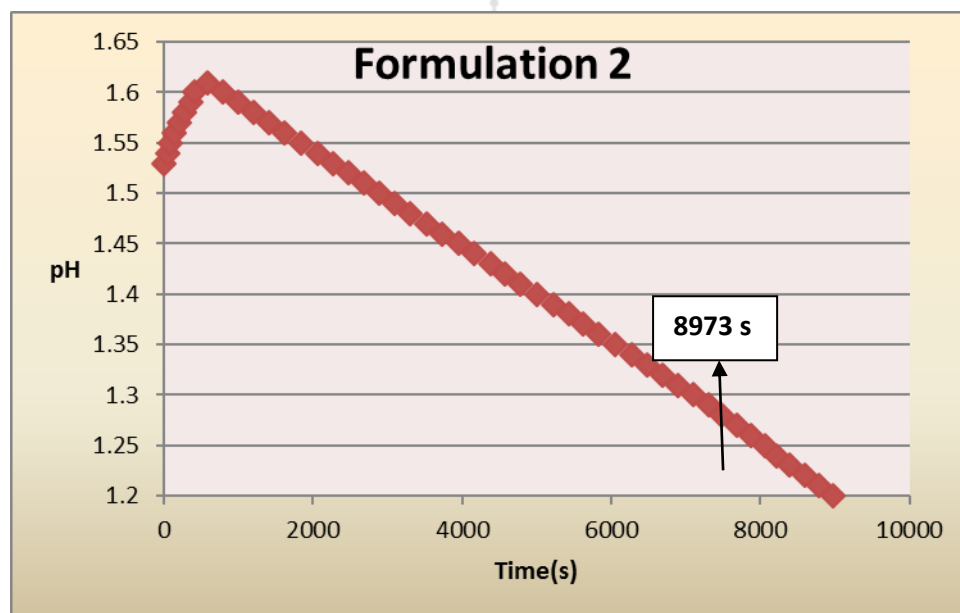


Figure No. 8: Duration of consistent neutralization of artificial gastric acid by Formulation 2.

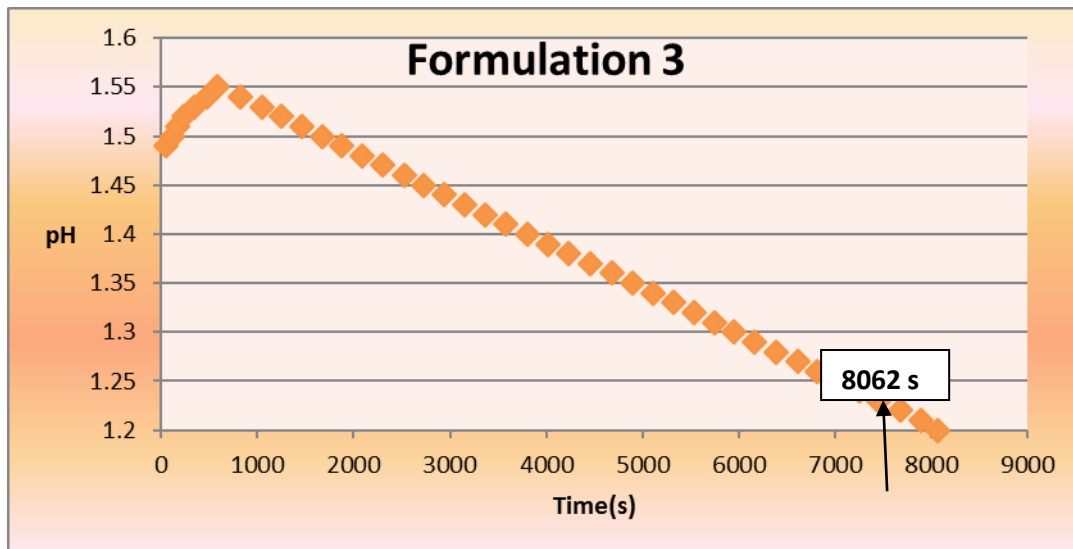


Figure No. 9: Duration of consistent neutralization of artificial gastric acid by Formulation 3.

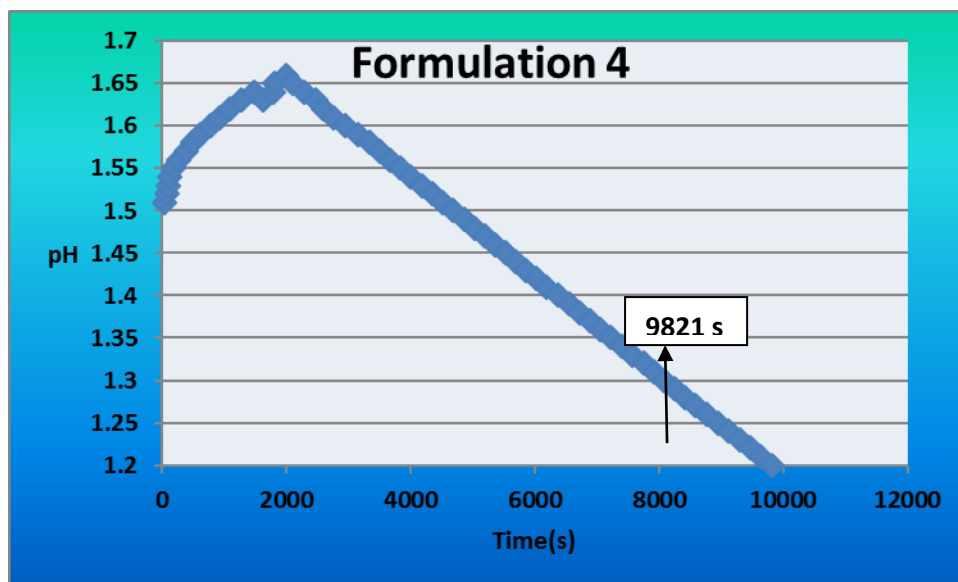


Figure No. 10: Duration of consistent neutralization of artificial gastric acid by Formulation 4.

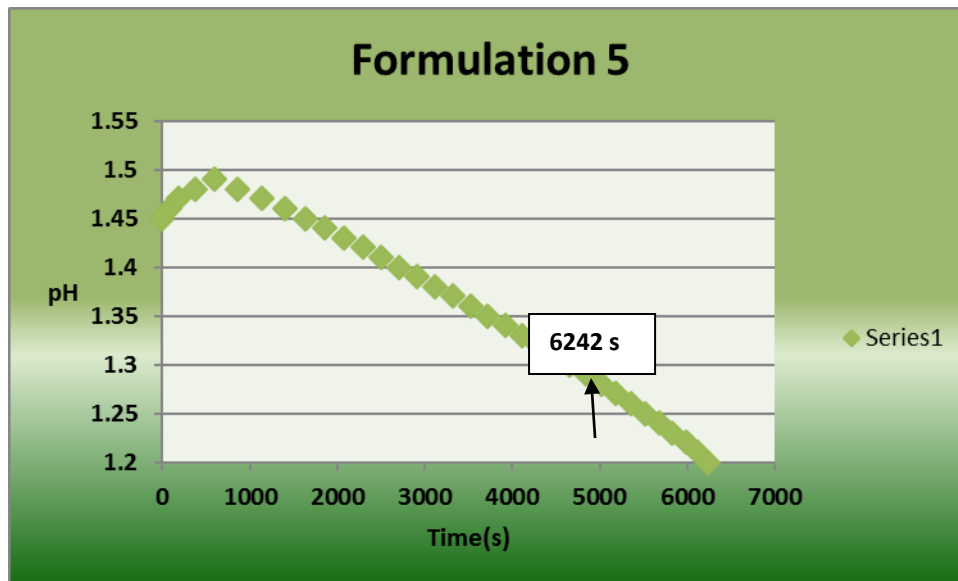


Figure No. 11: Duration of consistent neutralization of artificial gastric acid by Formulation 5.

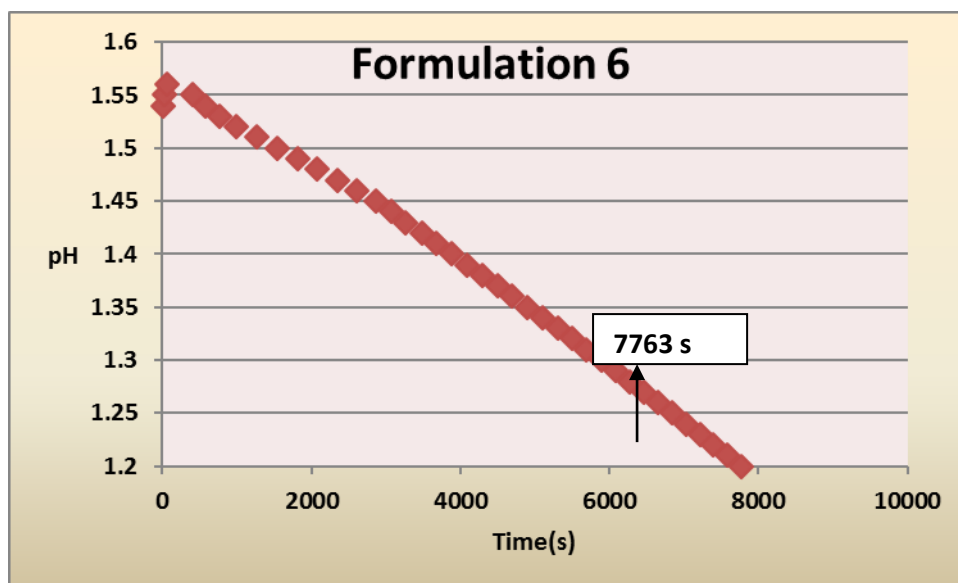


Figure No. 12: Duration of consistent neutralization of artificial gastric acid by Formulation 6.