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FORMULATION AND EVALUATION OF ALOE NIEBUHRIANA EXTRACT AS NATURACEUTICAL EFFERVESCENT GRANULES NOVEL DRUG DELIVERY SYSTEMS FOR ANTIDIABETIC ACTIVITY

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ABSTRACT

Ethnomedicine exhibits potential in developing affordable effective antidiabetic agents. The present study is based on the formulation of effervescent granules NDDS of Aloe niebuhriana latex extract. Six formulations were prepared using different acids, salts, diluents and superdisintegrants by the wet granulation method. The prepared granules were evaluated for flow property (like angle of repose, bulk density, tapped density, Hausner's ratio) pH, Effervescence time, and organoleptic properties studies. Effervescent granules have occupied a unique place in the field of pharmaceutics. Widely use in clinical diagnosis of heart burn, urinary tract infection, acidity. They contain one or more active pharmaceutical ingredient with or without excipients. Due to its onset of action will be get fast, so effervescent granules are mostly used. Effervescent granules are uncoated granules containing drug, acid substances, carbonates or hydrogen carbonate which rapidly react with water and liberate co_2. Six formulations containing the extract were prepared (F1–F6), and F6 containing 200 mg of the extract was selected for optimization due to its favorable odor, taste, foaming, and effervescent properties, high solubility, and absence of turbidity and adhesion. The formulated F6 granules successfully met the quality parameters assessed including flow time, pH effervescent time, angle of repose, bulk density, tapped density,

Carr's index, and Hausner's ratio. It was concluded that among the all formulations of A. niebuhriana extract effervescent granules NDDS the F6 was found to be as an optimized effervescent granules NDDS according to the formulation F6 exhibited effervescence time within 60 sec and successfully met the quality parameters, so the F6 was the best formulation of A. niebuhriana extract effervescent granules NDDS as an advanced phytotherapy approach for antidiabetic activity.

KEYWORDS: Aloe niebuhriana, Diabetes, Antidiabetic activity, Effervescent Granules NDDS, Herbal Formulation, Novel drug delivery systems.

INTRODUCTION

Background of Diabetes mellitus (DM)[1-12]

Diabetes mellitus (DM) stands as one of the most prevalent and serious chronic diseases of the current era, posing life threatening, disabling, and financially burdensome complications, and diminishing life expectancy. Indeed, diabetes is considered one of the five biggest morbidities worldwide. In 2021, it was estimated that 537 million people had diabetes, a figure projected to escalate to 643 million by the year 2030 and 783 million by the year 2045. Direct health expenditures due to diabetes are already close to one trillion USD and will exceed this figure by 2030. The International Diabetes Federation (IDF) Middle-East and North Africa Region has the highest percentage (24.5%) of diabetes-related deaths in people of working age. Notably, type 2 diabetes accounts for over 90% of all diabetes cases. While currently available antidiabetic medications are essential for managing glycemic levels, their use is often associated with significant side effects, including hypoglycemia, fluid retention, osteoporosis, and heart failure. These adverse effects can restrict their effectiveness in clinical practice. Consequently, there is an urgent demand for the development of novel antidiabetic therapies with fewer side effects to address diabetes and its related conditions, such as hyperglycemia, hyperinsulinemia, and hypertriglyceridemia. Natural products play a pivotal role in the development of novel medications that have enabled humanity combat several illnesses. Certain medicinal categories including antidiabetic drugs have greatly benefited from natural products. Phytomedicines offer not only cost-effective solutions to diseases but also safety. Traditional herbal medicines and functional foods are believed to ameliorate diabetic symptoms through multiple mechanisms of action, including enhanced insulin secretion and sensitivity, increased glucose uptake by muscle cells and adipose tissues, inhibition of glucose absorption from the intestines, reduced glucose production by

hepatocytes, and anti-inflammatory properties. As a result, functional foods and phytotherapies are becoming increasingly more popular across the world day by day. Nonetheless, there is a pressing need for scientific validation, standardization, and safety assessment of traditional medicinal plants before their recommendation for treating various ailments. Herbal medicine formulations, now produced by the modern pharmaceutical industry, are extensively available in the market for disease management public health enhancement. The categorization of finished herbal products into specific dosage forms aids in establishing precise protocols for quality control and stability testing.

Aloe Niebuhriana[13-22]

Aloe niebuhriana, belonging to the family Aloeaceae, is an indigenous species of Arabian Peninsula. Similar to Aloe vera, a widely recognized Aloe species, A. niebuhriana has a traditional application for treating multiple ailments such as hypertension, constipation, gastrointestinal parasites, and skin diseases as well as diabetes. Previous research indicates that A. niebuhriana contains anthra-glycoside, bitter principles, alkaloid, flavonoid, saponin, coumarins, aldehydes, phenols, tannins, and phytosterols. Furthermore, A. niebuhriana exhibits antioxidant and antimicrobial as well as hepatoprotective activities. In Yemen, medicinal plants are widely utilized for treating diseases in both humans and animals. However, only a handful of studies, often narrow in scope, have focused on documenting this indigenous knowledge. Given Yemen's vast geographical expanse and its diverse society, culture, and ecology, these studies represent only an initial yet crucial effort toward understanding and preserving the country's traditional medicinal practices. Similar to other rural societies, Yemeni people have historically maintained a deep connection with wild plants, using them for food, medicine, cosmetics, construction materials, shelter, and clothing. Yemen boasts a rich diversity of plants used in traditional medicine, including many indigenous and endemic plants. Investigating the antidiabetic properties of these traditional plants offers an opportunity to uncover new pharmacological applications and potential antidiabetic agents.

Novel Drug Delivery Systems[23-100]

Oral administration is the most popular route due to ease of ingestion, pain avoidance, versatility to accommodate various types of drug candidates, and, most importantly, patient compliance. Also, solid oral delivery systems do not require sterile conditions and are, therefore, less expensive to manufacture. Several novel technologies NDDS for oral delivery

have recently become available to address the physicochemical and pharmacokinetic characteristics of drugs, while improving patient compliance. Electrostatic drug deposition and coating. The most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, leading to patient incompliance particularly in case of pediatric and geriatric patients.

Granules Drug Delivery Systems

Granules are a unique type of dosage form which are composed of dried aggregates of powder solid particles which contain one or more Active Pharmaceutical Ingredients, with or without other ingredients.

Reasons for Granulation

To prevent segregation of the constituents of powder mix, to improve the flow properties of the powder mixture, to improve the compaction and compressibility characteristics of the powder mix, the granulation of toxic materials will reduce the hazard of the generation of toxic dust, which may arise during the handling of the powders, materials, which are slightly hygroscope, may adhere and form a cake if stored as a powder.

Effervescent Granules Novel Drug Delivery Systems

Effervescent Systems: This system NDDS uses carbonates (e.g. sodium bicarbonate) to generate in situ carbon dioxide (CO2). Organic acids (e.g. citric and tartaric acids) are added to speed up the reaction, thus reducing the density of dosage form and remaining buoyant in the stomach.

Effervescence

Effervescence is the release of CO2 gas in response to bicarbonates and acids in the presence of water. Sodium bicarbonate, potassium bicarbonate, sodium carbonate, and potassium are the bicarbonates used in the effervescent reaction. Other frequent acids employed in this reaction are citric, malic, tartaric, adipic, and fumaric acid. The acid-base reaction between citric acid and sodium bicarbonate is the most often occurring medication reaction in pharmaceutical application NDDS.

Effervescence is Latin word it means escape of gas escaping from an aqueous or water solution. Effervescent granules have short half-life as react rapidly with polar solvent or water. There is a liberation of carbon dioxide gas due to chemical reaction between acid and

base. Effervescent granules are a suitable dose form with excellent solubility, stability, and quick dissolving properties. These granules should be dissolved in a glass of water just before administration, and the resulting mixture or dispersion should be consumed right away as a result of the interaction between acid and base in the presence of water, the granules are rapidly distributed by the development of carbon dioxide in water.

Effervescent Granules NDDS are having high solubility, high stability, fast dissolving property and are also convenient dosage forms. They are coarse to very coarse powder containing of medicinal agent in a dry mixture usually composed of three primary parts; Active component, Acidic source (citric acid and tartaric acid) and alkaline substances (mainly carbonates/ bicarbonates) Granules can be packed as: Bulk granules or divided granules.

Advantages of Effervescent Granules NDDS

Rapid onset of action, pleasant taste, psychological effect, patient comfort to it, provide alkaline solution, neutralization of an acidic drugs as aspirin (alkalinization of urine and increase excretion of drug which is acidic).

Disadvantages of Effervescent Granules NDDS

Unstable (absorb the water moisture from the atmosphere), not accurate dose estimation because the one who estimate the dose is the patient himself, sodium overload (these granules are not suitable for hypertensive patients) and have many drug-drug interactions.

Benefits of Effervescent Granules NDDS

They include ease of administration, portability, a quicker start of action, gentler digestion, a superior taste, and greater stability compared to liquid dose forms, possibility for formulator to enhance flavor, a kinder effect on the stomach of the patient and marketing elements, higher bioavailability compared to alternative dosage forms, improved patient compliance, rapid onset of action, pleasant taste, reduced gastrointestinal irritation, prevent first-pass metabolism, granules have improved wetting, stability, flowability, and uniformity in particle size. The bioavailability of low absorbed drugs can be increased by effervescent granules preparation. Due to the high content of carbonate salt, upon the ingestion of drug solution, the gastric pH is temporarily elevated, resulting in first gastric emptying.

Effervescent Granules NDDS

Effervescent granules an effervescent dosage form, frequently tablets or granules, contains ingredients that, when in contact with water, rapidly release carbon dioxide, the dosage form NDDS is dissolved or dispersed in water to initiate the effervescence prior to ingestion. Effervescent salts are granules or coarse to very coarse powders containing a medicinal agent in a dry mixture usually composed of sodium bicarbonate, citric acid, and tartaric acid. When added to water, the acids and the base react to liberate carbon dioxide, resulting in effervescence. The resulting carbonated solution masks the undesirable taste of any medicinal agent. Effervescent granules are to be mixed in a glass of water and this solution or dispersion should be immediately drunk.

Uses of Effervescent Granules NDDS

It is easy to take the doses. The components, acid and carbonate, act as a pH-optimal buffer for the stomach. It offers both the extra liquid intake and the targeted medical benefit. Drinking effervescent tablet water with diarrhea and during hot summers helps increase daily fluid consumption. Benefits for patients with difficulty swallowing: Effervescent pills offer a substitute for these individuals. Easy handling and precise dosage measurement: Patients can receive precise dosages as effervescent dissolve fast. In effervescent granules a carbonate salt is neutralized by acid. Finally, a gas called carbon dioxide is released. Water has a key role in starting the reaction. Acid or carbonate cannot dissociate and the reaction cannot start if there is no water in the media. A greater amount of water is produced once the reaction starts. Effervescent granules need to be manufactured in the best possible conditions and packaged with care. As a result, stability is established. Anhydrous raw materials are used in the manufacture.

NDDS this in turn promotes drug adsorption from the upper small intestine, which is primary site of drug absorption. Effervescent granules are responsible for higher bioavailability and fast disintegration rates. Within a couple of minutes, the granules are completely dissolved and the drug become available in solution. The ideal disintegration time for effervescent granules is 6 to 9 sec. While disintegration time for uncoated tablet, coated tablet, film coated tablet and enteric coated tablet is 15min, 60min, 30min and 60min respectively.

NDDS are the removal of carbon dioxide gas from a fluid as a result of a chemical reaction is known as effervescence. When the preparation comes into touch with the water, which acts as a catalytic agent, this effect begins. The effervescent reaction yields carbon dioxide, which

enhances the absorption of active substances by allowing them to penetrate the paracellular route. Since the effervescent formulation avoids direct contact with the gastrointestinal tract, these dosage forms are beneficial for patients in this category.

Effervescent Active Ingredients

Citric Acid: Citric acid monohydrate's three carboxylate groups have varying pKa values: 3.15, 4.78, and 6.40 It serves as a pH regulator as well the most common type of citric acid available for purchase on the commercial market is monohydrate form. It is made by slowly evaporating cold, saturated liquids and crystallizing them. Saturated solutions of hot citric acid are used to create citric acid anhydrous. Citric acid and sodium bicarbonate-based effervescent formulations can produce a pleasing mouth feel experience on the tongue and in the mouth. It has been demonstrated that in effervescent formulations with citric acid, the disagreeable taste of functionalized calcium carbonate and calcium phosphate was covered up. Pharmaceutical formulations intended for oral administration frequently incorporate effervescence. The gas released when an acid and base react with water is referred to as "effervesce." Usually, sodium bicarbonate or sodium carbonate serves as the base and citric acid as the acid Carbonated liquid drinks can be made by mixing effervescent tablets or powders with water or another liquid, such saliva, to release carbon dioxide. Pharmaceuticals are administered with effervescence, which helps disperse active substances and facilitates rapid disintegration. This is especially useful for patients who have trouble swallowing tablets or capsules. Citric acid and bicarbonates react effervescingly, releasing CO2. This reaction is also utilized in the production of stomach floating tablets. The gel polymers of the tablet capture the CO2 gas created during the effervescent process, which causes buoyancy. Compared to ordinary tablets, the buoyant tablets float in the stomach's gastric fluid for a longer amount of time, allowing the medication to be absorbed by the stomach over longer periods of time and boosting its bioavailability.

Sodium Bicarbonate: Because of its strong reactivity, affordability, and high solubility, sodium bicarbonate is one of the most widely utilized carbonates. Therefore, water-soluble lubricants (such PEG 4000, 6000, and sodium benzoate), flavorings, sweeteners, and water-soluble colors are added as excipients. Compared to bicarbonate, sodium carbonate has a lower CO2 proportion. The CO2 content of bicarbonate is higher than that of soda ash. It is less steady and has a faster reaction time. The majority of goods employ a 50/50 ratio of

carbonate to bicarbonate. This form's response time and stability are adequate. Magnesium and potassium carbonate are also utilized in effervescent goods.

Tartaric Acid: White, crystalline, acidic powder known as tartaric acid. Pharmaceutical manufacture makes extensive use of tartaric acid and its derivatives. For instance, citrate and tartaric acid together can enhance the flavor of oral drugs. Tartaric acid has also been utilized to create effervescent salts.

Effervescent Systems for Delivering Herbal Active Ingredients

Effervescent systems NDDS provide a user-friendly and effective platform for delivering herbal actives. Nonetheless, several formulation hurdles persist. Herbal extracts often exhibit chemical instability, moisture sensitivity, and potential incompatibility with formulation excipients. While sweeteners and flavoring agents are commonly used to improve palatability, achieving complete taste masking without affecting the formulation's performance requires strategic excipient selection. Additionally, optimizing tablet attributes such as hardness, friability, and disintegration time, while maintaining antioxidant efficacy, involves a thorough understanding of how herbal constituents interact with gas-releasing agents and other excipients. Although interest in herbal effervescent formulations NDDS are expanding, there remains a lack of comprehensive literature summarizing key formulation parameters, associated challenges, and best practices for optimization. A deeper exploration of how various formulation components including acids, bases, binders, and sweeteners impact the overall quality, performance, and therapeutic potential of these dosage forms is crucial for future advancements.

Effervescent formulations NDDS and their benefits in herbal products Effervescent formulations are designed to undergo a chemical reaction upon dissolution in water, resulting in the release of carbon dioxide (CO_2). This effervescence facilitates rapid disintegration and can significantly enhance the solubility and subsequent bioavailability of the active constituents. These formulations are available in multiple delivery formats, offering versatility in drug design and patient use. The most widely used form is the effervescent tablet, which is formed through the compression of a formulation containing active ingredients and an acid. (such as citric or tartaric acid) and a base (commonly sodium bicarbonate or carbonate). Upon contact with water, the acid-base reaction generates CO_2, promoting immediate tablet breakdown and active ingredient dispersion. Effervescent granules function similarly but are provided in coarse or fine particle forms and are typically

packaged in moisture-resistant sachets, offering improved storage stability and convenience. Effervescent powders, characterized by smaller particle size, allow for even faster dissolution and are commonly applied in the context of herbal supplements. Less commonly, effervescent capsules have reactive powders that require removal from the capsule prior to dissolution; this form is particularly useful for sensitive actives that degrade in compressed forms. Additionally, effervescent liquids, where active ingredients are pre-dissolved in a solution that fizzes upon dilution, are used in specialized pharmaceutical applications. The diversity of these formats enables tailored formulation strategies that account for both pharmacokinetic and pharmacodynamic considerations. The increased adoption of effervescent dosage forms can be attributed in part to their streamlined manufacturing processes. Whether produced as powders, granules, or tablets, these formulations can be manufactured using conventional techniques such as direct compression, wet granulation, or dry granulation. Unlike traditional tablets or emulsified suspensions, effervescent products do not require advanced equipment for film coating, dispersion stabilization, or emulsification, reducing production complexity and cost. A key benefit of effervescent systems lies in their capacity to improve the bioavailability of poorly soluble herbal compounds.

The CO_2-driven reaction leads to the creation of a uniform aqueous solution, promoting enhanced dissolution and gastrointestinal absorption. This is especially advantageous for hydrophobic phytochemicals, such as flavonoids and polyphenols, which typically demonstrate limited oral bioavailability when administered in solid dosage forms.

Effervescent formulations NDDS are also especially advantageous for populations with swallowing difficulties, including pediatric, geriatric, or dysphagic patients. The liquid form of administration enhances ease of use and can be customized with flavoring agents and natural sweeteners to mask the often bitter or astringent taste of botanical ingredients, thereby improving palatability and patient adherence.

Pharmacokinetic of Effervescent Drug Delivery Systems

Pharmacokinetic advantages Effervescent NDDS provide several pharmacokinetic benefits over traditional oral solid dosage forms. One major advantage is the pre-dissolved state of the drug, which bypasses disintegration and promotes rapid absorption. The effervescent reaction between acid and base, such as citric/tartaric acid and sodium bicarbonate, produces CO_2 that aids in rapid dispersion and solution clarity. This reaction enhances drug availability and contributes to quicker onset of therapeutic effects, particularly beneficial for drugs requiring

rapid action. For poorly water-soluble drugs, wet granulation with hydrophilic binders like PVP facilitates better water penetration and enhances dissolution. Moreover, combining effervescence with gastric-floating mechanisms can improve drug residence time in the stomach, which is particularly useful for drugs with localized gastric absorption. Palatability is another key advantage of effervescent formulations. The fresh taste and ease of administration encourage patient adherence, especially for pediatric and geriatric populations.

Critical Effervescent Characterizations

Effervescence of NDDS are include onset time and duration of effervescence, which influence user experience and dosing reliability. Controlled CO_2 release ensures consistent dissolution without excessive foaming or gas loss. pH stability and buffering Maintaining an appropriate pH is essential for both API stability and bioavailability. The buffering capacity provided by components like citric acid and sodium bicarbonate ensures the pH remains within an acceptable range for absorption and drug integrity. Wettability and dispersion Efficient wetting and uniform dispersion prevent floating or sedimentation, especially in formulations containing poorly soluble APIs. These attributes are vital for dose uniformity and user acceptability. Carbonation and sensory properties Carbonation affects mouth feel and taste. While it can enhance palatability and mask bitterness, excessive foaming may lead to discomfort or dosage inconsistencies. A well-calibrated CO_2 level supports both compliance and therapeutic effectiveness. Stability and moisture sensitivity Effervescent formulations are highly prone to moisture. Packaging must protect against humidity induced premature reactions. Desiccants foil blisters, and airtight containers are typically employed. Additionally, chemical stability post-dissolution must be ensured. Gas pressure management Managing gas pressure both inside packaging and during dissolution is critical. Excess internal pressure can compromise product integrity, while rapid CO_2 buildup during administration may cause gastrointestinal discomfort. In future perspectives Effervescent formulations provide a promising platform for delivering herbal medicines, offering advantages in taste masking, absorption, and patient compliance.

Pharmaceutical Scientists are considering natural sources and medicinal herbs in the pharmaceutical industry an important part of drug development because natural sources of drugs have properties that are greater than industrial sources of drugs in NDDS. And the pharmaceutical industry strategies depend on the development of different pharmaceutical dosage forms and recent novel drug delivery systems. Using medicinal herbs and natural

sources as important goals of drug development. It is part of the art of innovation in drug development with different of novel drug delivery systems and pharmaceutical care for patients and society, it's the basic of development of the new pharmaceutical industry by developing different novel drug delivery systems from different sources.[50-91]

In the present study the A. niebuhriana extract develop into an effervescent granules NDDS was prepared and evaluated as an advanced phytotherapy approach for antidiabetic activity.

MATERIALS AND METHODS

Materials

The extract of *Aloe niebuhriana* was prepared and gift from (Prof. Dr. Bushra Abdulkarim Moharram, Professor Dr. of Pharmacognosy, Department of Pharmacognosy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen). Excipients including anhydrous citric acid, tartaric acids, stearic acid, sodium bicarbonate, sucralose, sodium saccharin, polyvinylpyrrolidone (PVP K-30), peppermint powder (menthol), simethicone, monopropylene glycol (MPG), Aerosil® 200, tween 20, sodium lauryl sulfate, and starch were generously provided by the Modern Pharma Company and Global Pharmaceutical Industries in Sana'a, Yemen. All other used reagents in this work were of analytical grade.

Equipment's

For formulation purposes, the following equipment was employed: a UV/VIS spectrophotometer (Cary 50 conc, Varian, USA), an FT-IR spectrometer (Scimitar 2000 FT-IR, Varian, USA), a PH meter (Metrohm 913, Swiss), a forced convection oven (model LDO-150F, Korea), a SCT SIONIC-6 sonicator bath (ScichemTech, USA), a hotplate stirrer (LMS-1003, Korea), a balance (Metler), and a Stuart SMP3 melting point apparatus (Barloworld Scientific Ltd., UK).

Antidiabetics Activity

α-Amylase Inhibition (In Vitro Study)

The inhibition assay was conducted following the methodology outlined in a previous study.[21]

Formulation and Evaluation of Effervescent Granules NDDS[50-130]

Formulation of Effervescent Granules

The effervescent granules of A. niebuhriana latex extract were prepared using the wet granulation method, Table 1 details the composition and quantities of each ingredient employed. Following the principles of geometrical dilution, all components were thoroughly mixed to ensure uniform dispersion of the extract. the resulting powder was then sieved through mesh no. 25. After that, a suitable amount of granulating agent (ethanol 99.9%) was added to form a moist mass. Tis moist mass was passed through sieve no. 16 to obtain granules. The granules formed were dried overnight in a hot air oven at 40°C and sealed in an airtight container.

Evaluation of Formulated Effervescent Granules

Evaluation of the Organoleptic and Physical Properties. The six effervescent formulations underwent assessment for their organoleptic properties, encompassing attributes such as shape, color, aroma, and taste. In addition, the physical properties of the granules, including foaming, adhesion, effervescence, turbidity, floating and solubility.

Table 1: The Composition of Aloe Niebuhriana Extract Effervescent Granules NDDS Formulations.

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Aloe Niebuhriana Extract	400	400	200	200	200	200
Sodium Bicarbonate	960	1750	1750	866.7	883.3	833.3
Citric Acid	430	833.3	766.7	366.7	333.3	383.3
Tartaric Acid	870	1666.7	1500	746.7	703.3	695
Sucralose	20	100	100	50	50	50
Sodium Lauryl Sulfate	6	---	---	---	---	---
Starch	300	---	---	---	---	---
Peppermint	14	23.3	23.3	10	16.7	16.7
Tween 20	---	60	166.7	---	30	30
Saccharin Sodium	---	166.7	166.7	80	83.3	83.7
Ascorbic Acid	---	---	26.7	---	---	---
Aerosil	---	---	100	80	50	83.3
Simethicone	---	---	---	50	50	50
Stearic Acid	---	---	---	50	---	---
Monopropylene Glycol	---	---	---	---	50	50
PVP K-30	---	---	---	---	50	25

Flowability Study

The flowability test was conducted only on the formulation that exhibited satisfactory results in the organoleptic and physical tests. Employing the funnel method, the flow rate and angle

of repose were measured. A funnel was positioned on either a ring support stand or a lambed stand, adhering to pharmacopeial standards for height. Approximately, 10 g of the granule sample was placed in the funnel with the bottom hole closed. Subsequently, the lower lid of the funnel is opened to allow the granules to descend onto a level surface, forming a conical pile. The flow time duration from the initiation of granule flow until cessation was recorded using a stopwatch. The flow rate of the sample and the angle of repose of the sample were calculated as follows:

Flow rate = Weight (grams) /Time (seconds).

The angle of repose was calculated using the following formula:

$\text{Tan}\theta = h/r^2$ where θ represents the angle of repose, h represents the height of the formed pile cone, and r represents the radius of the base of the cone.

Bulk Density (BD) and Tapped Density (TD)

Two types of density, namely, BD and TD, were determined. A measured quantity of granules was placed into a measuring cylinder, and the initial volume was recorded to determine the BD. Subsequently, the measuring cylinder was subjected to tapping at a rate of 100 taps per minute until maximum packing was achieved. The powder level in the measuring cylinder was checked after every 10 taps until no further reduction in volume occurred.

BD and TD were then calculated using the following formulas: BD = Granules weight /Packing volume,

TD = Granules weight /Tapped volume of packing. To assess the flow properties and compressibility of the effervescent granules derived from A. niebuhriana extract, Carr's Index (CI) and Hausner Ratio (HR) were determined.

These were calculated using the equations:

$CI = (TD - BD /TD) \times 100$,

$HR = TD /BD$.

Effervescence Time

The effervescent time for the granules was determined by introducing a single dose (2.5 g) of the A. niebuhriana extract effervescent granules into a glass containing 200 mL of water, and the duration time until effervescent cessation was recorded.

pH Test

For the pH test, the effervescent solution was prepared by dissolving 2.5 g of the granules in 100 mL of water, followed by pH measurement using a pH meter. A pH reading within the range of 6 to 7 is considered optimal for the effervescent solution, indicating neutrality.

Packing of the Finished Product

The optimized effervescent granules formulation was prepared and packed.

RESULTS AND DISCUSSION

In this study, the extract was formulated into effervescent granules. Six formulations were prepared using the wet granulation method, each containing a combination of various ingredients listed in Table 1. The ingredients across the six formulations were included different amounts of the extract, citric acid, tartaric acids, stearic acid, sodium bicarbonate, sucralose, sodium saccharin, PVP K-30, peppermint powder (menthol), simethicone, MPG, aerosil® 200, tween 20, sodium lauryl sulfate, and starch. As shown in Table 2, the organoleptic and other physical properties of the six prepared formulations. The properties evaluated included foaming, adhesion, effervescence, turbidity, floating and solubility. Based on these properties.

Table 2: The Organoleptic and Physical Properties of the Six Aloe Niebuhriana Extract Effervescent Granules NDDS Formulations.

Tests	F1	F2	F3	F4	F5	F6
Color	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Odor	Moderate	Moderate	Good	Good	Good	Good
Taste	bad	Good	Good	Good	Good	Good
Foaming	High	High	High	Moderate	Good	Good
Adhesion	+	+	_	+	+	_
Effervescence	Good	High	Good	Good	Good	Good
Turbidity	High	Clear	Clear	Clear	Clear	Clear
Solubility	Poor	Poor	Moderate	Moderate	High	High

Formulation (F6) was selected for further optimization due to favorable qualities such as odor, taste, foaming, high solubility properties with no formation of apparent turbidity or adhesion. Figure 1 displays the formulated effervescent granule (F6). This chosen formulation (F6) contained the following components: extract (200 mg), Na bicarbonate (833.3 mg), citric acid (383.3 mg), tartaric acid (695.0 mg), sucralose (50 mg), peppermint (16.7 mg), tween 20 (30.0 mg), Na saccharin (83.3 mg), aerosil (50.0 mg), simethicone (0.3 g), MPG (0.3 g), and PVP K30 (0.15 g). 3.4. Evaluation of the A. niebuhriana Effervescent

Granules. Table 3 summarizes the evaluation of F6 for its pH, effervescent time, flow time, angle of repose, BD, TD, Carr's index, and Hausner's ratio. The granules were observed to be yellow in color, with a pleasant peppermint odor and taste.

Fig. 1: An Image of the Formulated Effervescent Granules from A. niebuhirana Extract.

The results of the evaluation revealed the following parameters for the formulated effervescent granules: pH of 5.28, angle of repose of 24.4°, BD of 0.62 g/mL, TD of 0.72 g/mL, Carr's index of 14.29, Hausner ratio of 1.17, and effervescent time of 60 sec.

Table 3: Physical Characteristics of Formulation (F6) Effervescent Granules NDDS.

Physical characteristic	Results
Flow time (g/sec)	10
Angle of repose	24.4
Bulk density(g/mL)	0.62
Tapped density(g/mL)	0.72
Carr's index	14.29
Hausner ratio	1.17
pH	5.28
Effervescent Time (sec)	60
Color	Yellow
Odor	Peppermint
Taste	Peppermint

DISCUSSION

Herbal Formulations Development[100-137]

Per the World Health Organization (WHO), over 60% of the global populations continue to depend on herbal medicine to address both short-term and chronic ailments. Owing to extensive usage, numerous pharmaceutical companies have ventured into producing diverse herbal formulations. The growing acceptance of herbal formulations is attributed to their

affordability, efficacy, and lower toxicity profile. Ensuring the effectiveness, therapeutic efficacy, quality, and adherence to product standards are important considerations for any herbal formulation. In the present study, A. niebuhriana latex extract was formulated and optimized as effervescent granules. Effervescent granules NDDS, comprising a mix of acids and bases, exhibit a unique property: when dissolved in water, they generate foam and mimic the taste of soft drinks. Effervescence is known to enhance the dissolution and aids in masking the unpleasant taste and offer a refreshing experience when consumed. In our study, six effervescent formulations were prepared containing 200 or 400 mg of the plant extract, since these two doses were shown effective to manage diabetic symptoms in rats. The goal was to produce effervescent granules utilizing a combination of citric acid and tartaric acid as acid-forming effervescent salts. This combination yielded granules of superior quality, characterized by a neither nonstick and nonbrittle texture. For the base-forming effervescent salt component, we employed sodium bicarbonate, which proved to generate a substantial amount of carbon dioxide (CO2) during the effervescent reaction. These measures have proved effective in heightened user preference. Tween 20 and SLS served as dispersing and wetting agents in our formulation. Notably, Tween 20 exhibited lower foaming tendencies compared to SLS. Sucralose and sodium saccharin were used as sweeteners, while peppermint powder, Aerosil 200, simethicone, povidone, and MPG were added to enhance favor, improve powder fow, mitigate foam formation, act as a binder, and assist in wetting, respectively. To ensure uniformity and homogeneity of the powder mixture, the blend of extract powder and excipients underwent sieving using a mesh size of 25 to break up powder clumps. Absolute ethanol (99.9%) served as a granulating agent due to its nonactivation of the effervescent reaction and its easy removal from the wet granules at low temperatures. After that, the dried granules were sieved through a mesh size of 16 to yield identical granules characterized by flow well properties and minimal weight variation when filled. The flow time of 100 g of granules ≤ 10 s, as observed in our investigation, indicates a favorable flow rate as demonstrated by the flow rat test. Moreover, an angle of repose falling within the range of 20°–30° indicates favorable flow properties, while angles of repose exceeding 40° suggest poor flow properties. In this study, the formulated extract granules had an angle of repose 24.4°, indicating good flow properties. Furthermore, a Hausner ratio serves as another indicator of flow properties, with values below 1.25 indicative of good flow and values above 1.6 suggesting poor flow. Our prepared formulation had a Hausner ratio of 1.17, confirming the granules favorable flow properties. Adjusting the pH of the effervescent solution is crucial to minimize gastrointestinal irritation. Overly acidic effervescent solutions can

potentially irritate the stomach. Conversely, alkaline solution may impart a bitter taste. The pH value of the selected formulation (F6) was 5.28, which falls within the desirable range close to neutral.

Effervescence time, on the other hand, refers to duration it takes the granules to fully dissolve into solution and produce gas. In the current study, the value of effervescence time of the selected formulation (F6) was 60 s, which falls within the acceptable range according to USP. The granules of F6 exhibited a distinctive yellow color and emitted a characteristic mint odor and taste. To preserve the quality of these granules, they were packaged into special sachets comprising four layers: polyvinyl, aluminum, paper, and polyvinyl. These sachets offer impermeability to moisture and possess weak heat conduction properties, thereby safeguarding the integrity of the product. The study demonstrates strengths in its comprehensive approach, assessing both in vitro and in vivo antidiabetic effects of A. niebuhriana latex and innovatively developing an effervescent granule NDDS formulation to improve practicality and user compliance.

CONCLUSION

The study demonstrates that the successful formulation of A. niebuhriana latex extract formulations as effervescent granules NDDS via the wet granulation method highlights the potential for its pharmaceutical application. effervescent granules are a common dosage form that have various advantages. They have a quicker beginning of action and improved bioavailability since they dissolve easily in water and are absorbed by the body. They taste better and are more convenient for people who have trouble swallowing, which improves patient compliance. The six formulations effervescent granules NDDS were prepared by the wet granulation technique that contains A. niebuhriana extract, citric acid, tartaric acids, stearic acid, sodium bicarbonate, sucralose, sodium saccharin, PVP K-30, peppermint powder (menthol), simethicone, MPG, aerosil 200, tween 20, sodium lauryl sulfate, and starch. It was concluded that among the all formulations of A. niebuhriana extract effervescent granules NDDS the F6 was found to be as an optimized effervescent granules NDDS according to the formulation F6 exhibited effervescence time at 60 sec and successfully met the quality parameters, so the F6 was the best formulation of A. niebuhriana extract effervescent granules NDDS as an advanced phytotherapy approach for antidiabetic activity.

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REFERENCES

1. A H Heald, M Stedman, M. Davies, et al. Estimating Life Years Lost to Diabetes: Outcomes from Analysis of National Diabetes Audit and Office of National Statistics Data. Cardiovascular Endocrinology & Metabolism., 9, 2020; 9(4): 183–185.
2. A T Kharroubi, H M Darwish. Diabetes Mellitus: The Epidemic of the Century, World Journal of Diabetes, 2015; 6: 850–867.
3. H Sun, P Saeedi, S Karuranga, et al. IDF Diabetes Atlas: Global, Regional and Country-Level Diabetes Prevalence Estimates for 2021 and Projections for 2045. Diabetes Research and Clinical Practice, 2022; 183: 109-119.
4. D. Magliano, E Boyko. IDF DIABETES ATLAS (International Diabetes Federation., 2021.
5. M Laakso. Biomarkers for Type 2 Diabetes. Molecular Metabolism., 27 2019; 27: S139–S146.
6. O J Phung, J M Scholle, M Talwar, C I Coleman. Effect of Noninsulin Antidiabetic Drugs Added to Metformin Therapy on Glycemic Control, Weight Gain, and Hypoglycemia in Type 2 Diabetes. JAMA., 2010; 303(14): 1410–1418.
7. D Ghosh, P Parida. Drug Discovery and Development of Type 2 Diabetes Mellitus: Modern-Integrative Medicinal Approach. Current Drug Discovery Technologies., 2016; 13: 60–67.
8. Y-E Joo. Natural Product-Derived Drugs for the Treatment of Inflammatory Bowel Diseases. International Researchers., 2014; 12(2): 103–109.
9. G Li, A Kam, K Wong, et al. Herbal Medicines for the Management of Diabetes. Advances in Experimental Medicine and Biology., 2012; 771: 396–413.
10. M I Kazeem, T C Davies. Anti-diabetic Functional Foods as Sources of Insulin Secreting, Insulin Sensitizing and Insulin Mimetic Agents. Journal of Functional Foods., 2016; 20: 122–138.
11. P Sabale, B Bhimani, C Prajapati, V Sabalea. An Overview of Medicinal Plants as Wound Healers. Journal of Applied Pharmaceutical Science., 2012; 2: 143–150.
12. Who. Stability Testing of Active Substances and Pharmaceutical Products. Restricted Work. Doc. QAS/06., 2006; 179: 10–32.

13. A Al-Khulaidi. The Sustainable Natural Resource Management Project (SNRMP II) EPA and UNDP., 2013.
14. M Tanaka, E Misawa, Y Ito, et al. Identification of Five Phytosterols from Aloe Vera Gel as Anti-diabetic Compounds. Biological and Pharmaceutical Bulletin., 2006; 29(7): 1418–1422.
15. B Moharram, A Al-Doaiss, H Al-Mahbashi, et al. Hepatoprotective, Antioxidant and Cytotoxic Potential of Aloe Niebuhriana Latex Extract from Yemen. Indian Journal of Pharmaceutical Sciences., 2020; 82(3): 514–521.
16. J Fleurentin, JM Pelt. Repertory of Drugs and Medicinal Plants of Yemen. Journal of Ethnopharmacology., 1982; 6(1): 85–108.
17. J Fleurentin, JM Pelt. Additional Information for a Repertory of Drugs and Medicinal Plants of Yemen. Journal of Ethnopharmacology., 1083; 8(2): 237–243.
18. Fleurentin, G Mazars, JM Pelt. Additional Information on the Cultural Background of Drugs and Medicinal Plants of Yemen," Journal of Ethnopharmacology., 1983; 8(3): 335–344.
19. M Al-Fatimi. The Scope of the Pharmaceutical Industry from Indigenous Medicinal Plants (The Medicinal Plants of Yemen). Yemeni Studies (Dirasat Yamaniyyah)., 1992; 44: 424–445.
20. N H Nguyen, Q T Pham, T N H Luong, H K Le, V G Vo. Potential Antidiabetic Activity of Extracts and Isolated Compound from Adenosma Bracteosum (Bonati). Biomolecules., 2020; 10(2): 201.
21. B A Moharram, H M AL-Mahbashi, T Al-Maqtari, R Saif-Ali, I A Al-Hakami, W T Alhaj. Leaves of Capparis Cartilaginea Exhibit a Promising Antidiabetic Activity in Alloxan-Induced Diabetic Rats. International Journal of Pharmaceutical Research and Allied Sciences., 2023; 12(4): 65–75.
22. B A Moharram, MM Alburyhi, T Al-Maqtari, A Faisal. Evaluating the Antidiabetic Activity of Aloe niebuhriana Latex in Alloxan-Induced Diabetic Rats and the Development of a Novel Effervescent Granule-Based Delivery System. The Scientific World Journal., 2025; 1-13.
23. Ranade A, Ramesh C, Ranpise N. Enrichment of antiulcer activity of monoammonium glycerrhizin and Aloe vera gel powder through a novel drug delivery system. Asian J Pharm., 2014; 8(4): 222.
24. Loyd VA, Nicholas CP, Howard CA. Ansel's Pharmaceutical dosage form and drug delivery system. Edn 9, Lippincott Williams and Wilkins, Philadelphia., 2011; 198-200.

25. Surini S, Wardani MRW, Sagita E. Evaluating of effervescent tablets containing grape seed (Vitisvinifera l.) Extract as a nutraceutical. Int J Appl Pharm., 2017; 9: 150.
26. Patel JB, Suhagia BN, Patel MN, Patel BT, Patel AM, Patel TR. Preparation and evaluation of effervescent tablets of ibuprofen. WJPPS., 2013; 2(4): 2145-2155.
27. Pietta P, Minoggio M, Bramati L. Plant Polyphenols: Structure, Occurrence and Bioactivity., In 2003; 257–312.
28. Srinath KR, Chowdary P, Palaniswamy P, VamsyKrishna A, Aparna S, Ali SS et al. Formulation and evaluation of effervescent tablets of Paracetamol. IJPRD., 2011; 3(3): 76-104.
29. Friedman M, Jürgens HS. Effect of pH on the Stability of Plant Phenolic Compounds. J Agric Food Chem., 2000; 48(6): 2101–10.
30. Rajalakshmi G, Vamsi CH, Balachander R, Damodharan N. Formulation and evaluation of diclofenac potassium effervescent tablets. Int J Pharm Biomed Res., 2011; 2(4): 237- 243.
31. Hahidi F, Hossain A. Importance of Insoluble- Bound Phenolics to the Antioxidant Potential Is Dictated by Source Material. Antioxidants., 2023; 12(1): 203.
32. Raymond CR, Paul JS, Marian EQ. Handbook of Pharmaceutical excipients. Edn 6, RPS publishing, UK., 2009; 424-425.
33. Purbowati ISM, Maksum A, Anggriawan R. Effervescent formulation based on variation of nanocapsules matrix type and roselle (Hibiscus sabdariffa) nanocapsules percentage. Food Res., 2021; 5(3): 53–9.
34. K Divya, G Vamshi, T Vijaykumar, M sandhtay Rani, B Kishore. Review on introduction to effervescent tablet and granules. kenkyu journal of pharmacology., 2020; 2455 – 9237.
35. Venkatachalam CD, Sengottian M, Sengodan T. Formulation and evaluation of polyherbal floating effervescence tablet containing Pedalium murex and Tribulus terrestris fruit extracts. Int J Appl Pharm., 2017; 9(2): 10.
36. Adi-Dako ofosua, Christina Kumadoh Doris, Egbi Godfred, Okyem Samuel, Addo Yaw Papa, Nyarlo Alexander, Asare osei. Oppong Eshun Esther, Adase Emmanule. Strategies for formulation of effervescent granules of an herbal product for the management of typhoid fever., 2021; 7(10): e08147.
37. Suksaeree J, Monton C, Charoenchai L, Chankana N, Wunnakup T. Optimization of Process and Formulation Variables for Semha–Pinas Extract Effervescent Tablets Using the Box–Behnken Design. AAPS PharmSciTech., 2023; 24(1): 52.

38. British Pharmacopeia commission. British Pharmacopeia 2016. Append. XIII Part. Contam. Sub-visible Part., 2016; 1069.
39. Gustaman F, Amin S, Nurdianti L, Wulandari WT, Idacahyati K, Nurlathifah L. Antioxidant activity of effervescent granules from kirinyuh leaves (Chromolaena odorata (l.) R. M. King and h. Rob) and leaf of mareme (Glochidion arborescens blume). Int J Appl Pharm., 2022; 26: 86–91.
40. Patel AA, Parikh RH, Mehta TA. Mehta. Development optimization and evaluation of effervescent tablets of chloeniramine maleate using box Behnken design.International Journal of Pharmaceutical Sciences., 2015; 8(8): 317– 323.
41. Singh M, Sharma D, Kumar D, Singh G, Swami G, Rathore MS. Formulation, Development, and Evaluation of Herbal Effervescent Mouthwash Tablet Containing Azadirachta Indica (Neem) and Curcumin for the Maintenance of Oral Hygiene. Recent Pat Drug Deliv Formul., 2020; 14(2): 145–61.
42. Aulifa DL, Wibowo DP, Safitri N, Budiman A. Formulation of effervescent granules from red ginger (Zingiberis officinale roscoe var. Rubrum) extract and its antioxidant activity. Int J Appl Pharm., 2022; 7: 112–5.
43. Iveson SM, Litster JD, Hapgood K, Ennis BJ. Nucleation, growth and breakage phenomena in agitated wet granulation processes: a review. Powder Technology., 2001; 117: 3–39.
44. Maysarah H, Sari I, Faradilla M, Kwok K. Formulation of effervescent granule from robusta green coffee bean ethanolic extract (Coffea canephora). J Pharm Bioallied Sci., 2020; 12(6): 743.
45. Satapathy SR, Patra M, Patnaik M. Process and variation in effervescent formulation: A review. Innovint J Med Pharm Sci., 2016; 1: 1-3.
46. Ranade AN, Wankhede SS, Ranpise NS, Mundada MS. Development of Bilayer Floating Tablet of Amoxicillin and Aloe vera Gel Powder for Treatment of Gastric Ulcers. AAPS PharmSciTech., 2012; 13(4): 1518–23.
47. Prabhakar C, balakrishna K. Preparation and evaluation of effervescent tablets of paracetamol. A review on effervescent tablets. Int J Pharm Tech., 2011; 3: 704712.
48. Ain MRF, Yusof YA, Chin NL, Amin NAM, Ghazali HM. Optimisation of an Effervescent Pineapple Tablet. J Biol Sci., 2016; 16(7): 247–55.
49. Forestryana D, Abdurrahman, Ramadhan H. Effervescent tablet formulation ethanol extracts 70% kelakai root (Stenochlaenapalutris (burm. F.) Bedd.) with variation concentration of gas generating agent. Int J Appl Pharm., 2022; 1: 10–6.

50. Bary AA, El-Gazayerly ON, Alburyhi MM. A Pharmaceutical Study on Lamotrigine. Ph.D. Thesis, Faculty of Pharmacy, Cairo University., 2009.
51. Alburyhi MM, Salim YA, Saif AA, Noman MA. Furosemide-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(22): 1178-1219.
52. Alburyhi MM, Saif AA, Noman MA. Lornoxicam-Excipient Compatibility Studies for Microsponge-Based Drug Delivery Systems Development. World Journal of Pharmaceutical and Medical Research., 2025; 11(4): 70-81.
53. Hamidaddin MA, Alburyhi MM, Noman MA, Saif AA. Formulation and Evaluation of Rosuvastatin Fast Dissolving Tablets. World Journal of Pharmacy and Pharmaceutical Sciences., 2023; 12(9): 2293-2303.
54. Alburyhi MM, Hamidaddin MA, Noman MA, Saif AA, Yahya TA, Al-Ghorafi MA. Rivaroxaban-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. European Journal of Pharmaceutical and Medical Research., 2024; 11(9): 370-404.
55. Bary AA, El-Gazayerly ON, Alburyhi MM. Formulation of Immediate Release Lamotrigine Tablets and Bioequivalence Study. Journal of Chemical Pharm Research., 2013; 5(10): 266–271.
56. Saif AA, Alburyhi MM, Noman MA, Yahya TA, Al-Ghorafi MA. Famotidine-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(18): 1346-1408.
57. Alburyhi MM, Noman MA, Saif AA, Al-Ghorafi MA, Al Khawlani MA, Yahya TAA. Formulation and Evaluation of Anti-acne Spironolactone Emulgel Novel Trend in Topical Drug Delivery System. World Journal of Pharmaceutical Research., 2023; 12(22): 96-119.
58. Alburyhi MM, Noman MA, Saif AA, Salim YA, Hamidaddin MA, Yahya TA, Al-Ghorafi MA, Abdullah JH. Lisinopril-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(16): 59-111.
59. Al-Ghorafi MA, Alburyhi MM, Saif AA, Noman MA, Yahya TA. Drotaverine-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(18): 1285-1340.
60. Alburyhi MM, Noman MA, Saif AA, Hamidaddin MA, Yahya TA, Al-Ghorafi MA. Rosuvastatin Calcium-Excipient Compatibility Studies for Advanced Drug Delivery

Systems Development. World Journal of Pharmaceutical Research., 2024; 13(13): 1549-1582.

61. Alburyhi MM, Saif AA, Noman MA. Ticagrelor-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(10): 1081-1132.
62. Alburyhi MM, Noman MA, Saif AA, Al-Ghorafi MA, Yahya TA, Yassin SH, AlKhawlani MA. Diclofenac-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(14): 1297-1333.
63. Alburyhi MM, Saif AA, Noman MA, Salim YA, Hamidaddin MA. Formulation and Evaluation of Lisinopril Orally Disintegrating Tablets. World Journal of Pharmacy and Pharmaceutical Sciences., 2023; 12(9): 357-369.
64. Alburyhi MM, Saif AA, Noman MA. Stability Study of Six Brands of Amoxicillin Trihydrate and Clavulanic Acid Oral Suspension Present in Yemen Markets. Journal of Chemical Pharm Research., 2013; 5(5): 293-296.
65. Alburyhi MM, Hamidaddin MA, Saif AA, Noman MA. Formulation and Evaluation of Rivaroxaban Orodispersible Tablets. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(2): 2066-2092.
66. Alburyhi MM, Saif AA, Noman MA, Yahya TA. Formulation, Development and Evaluation of Famotidine Orodispersible Tablets. European Journal of Pharmaceutical and Medical Research., 2023; 10(10): 56-62.
67. Aboghanem A, Alburyhi MM, Noman MA. Effect of Different Excipients on Formulation of Immediate Release Artemether/Lumefantrine Tablets. Journal of Chemical Pharm Research., 2013; 5(11): 617-625.
68. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Celery Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Gout. World Journal of Pharmaceutical Research., 2024; 13(11): 2383-2404.
69. Raweh SM, Noman MA, Alburyhi MM, Saif AA. Formulation and Evaluation of Anti-acne Gel of Azadirachta Indica Extract Herbal Product. European Journal of Pharmaceutical and Medical Research, 2024; 11(2): 427-433.
70. Alburyhi MM, Saif AA, Noman MA. Formulation and Evaluation of Ticagrelor Orodispersible Tablets. World Journal of Pharmaceutical Research., 2024; 13(5): 26-55.

71. Alburyhi MM, Saif AA, Noman MA, Yahya TA, Al-Ghorafi MA. Formulation and Evaluation of Drotaverine Orally Disintegrating Tablets. World Journal of Pharmaceutical Research., 2023; 12(18): 66-79.
72. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Effervescent Granules of Artemisia Arborescence Herbal Product for Foodborne Illness. World Journal of Pharmacy and Pharmaceutical Sciences., 2023; 12(12): 1429-1444.
73. Alburyhi MM, Noman MA, Saif AA. Formulation and Evaluation of Natural Herbal Anti-acne as Gel Delivery Systems. World Journal of Pharmaceutical Research., 2024; 13(21): 1447-1467.
74. Alburyhi MM, Noman MA, Alemad AF. Preformulation Studies of Cefixime for Dispersible Tablets Delivery System Development. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(12): 75-99.
75. Noman MA, Alburyhi MM, Saif AA, Yahya TAA. Formulation and Evaluation of Polyherbal Extract for Skin Hyperpigmentation as Gel Advanced Delivery Systems. World Journal of Pharmaceutical Research., 2024; 13(22): 1260-1280.
76. Alburyhi MM, Noman MA, AA Saif. Formulation and Evaluation of Meloxicam Emulgel Delivery System for Topical Applications. World Journal of Pharmaceutical Research., 2025; 14(4): 1324-1337.
77. Othman AM, Alburyhi MM, Al-Hadad GH. Formulation and Evaluation of Captopril Mouth Dissolving Tablets. European Journal of Pharmaceutical and Medical Research, 2024; 11(1): 18-28.
78. Alburyhi MM, Noman MA, Saif AA, Alemad AF. Dispersible and Orodispersible Tablets Delivery Systems for Antibacterials Development. World Journal of Pharmaceutical Research., 2025; 14(1): 1229-1257.
79. Al-Ghorafi MA, Alburyhi MM, Saif AA, Noman MA. Meloxicam-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical and Medical Research., 2025; 11(1): 87-106.
80. Alburyhi MM, Saif AA, Noman MA. Domperidone-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Biomedical and Pharmaceutical Sciences., 2025; 12(3): 250-269.
81. Alburyhi MM, Saif AA, Noman MA. Spironolactone-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmacy and Pharmaceutical Sciences., 2025; 14(3): 871-910.

82. Saif AA, Alburyhi MM, Noman MA. Ketoprofen-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmacy and Pharmaceutical Sciences., 2025; 14(4): 92-123.
83. Alburyhi MM, Saif AA, Noman MA, Yassin SH. Formulation and Evaluation of Simvastatin Orodispersible Tablets. World Journal of Pharmaceutical Research., 2023; 12(16): 1033-1047.
84. Alburyhi MM, Saif AA, Noman MA, Saeed SA, Al-Ghorafi MA. Formulation and Evaluation of Diclofenac Orodispersible Tablets. European Journal of Pharmaceutical and Medical Research., 2023; 10(9): 01-06.
85. Alburyhi MM, Noman MA, Saif AA. Metronidazole-Excipient Compatibility Studies for Medicated Chewing Gum Delivery Systems Development. European Journal of Pharmaceutical and Medical Research., 2025; 12(4): 567-589.
86. Alburyhi MM, Saif AA, Noman MA, Alkhawlani MA. Formulation and Evaluation of Bisoprolol Fast Dissolving Tablets. World Journal of Pharmaceutical Research., 2023; 12(16): 01-10.
87. Alburyhi MM, Noman MA, Saif AA, Salim YA, Abdullah JH. Formulation and Evaluation of Domperidone Orodispersible Tablets. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(3): 49-68.
88. Alburyhi MM, Saif AA, Noman MA, Hamidaddin MA. Formulation and Evaluation of Clopidogrel Orodispersible Tablets. World Journal of Pharmaceutical Research., 2024; 13(6): 42-64.
89. Alburyhi MM, Saif AA, Noman MA, Al Khawlani MA. Bisoprolol-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical and Medical Research., 2024; 10(10): 304-324.
90. Bary AA, El-Gazayerly ON, Alburyhi MM. A Pharmaceutical Study on Methocarbamol. MSc Thesis, Faculty of Pharmacy, Cairo University., 2006.
91. Saif AA, Alburyhi MM, Noman MA. Formulation and Evaluation of Ketoprofen Fast Dissolving Tablets. International Journal of Sciences., 2018; 7(09): 27-39.
92. Bhavana Dnyandeo Tambe, Formulation and Evaluation of Paracetamol Effervescent Tablet, Research Article, Asian Journal of Pharmaceutical Research and Development., 2021; 9(4): 47-51.
93. Bala R, Badjatya S, Madaan R. Strategies practiced to perk up oral palatability and acceptance of bitter drugs, J Drug Deliv Sci Technol., 2020; 56: 101580.

94. Sangram Biranje, Akshata More, Trusha P. Shangrapawar, Ashok Bhosale, A Review on Formulation and Evaluation of Effervescent Tablet, Review Article, IJPPR., 2021; 21(3).
95. Jadhav S, Gangurde A. A Bird Eye View on Effervescent Drug Delivery System. Int J Drug Deliv Technol., 2023; 13(3): 1046–58.
96. Kalyani Waghchoure, A Review on: Effervescent Tablet, IJPRA., 2023; 8(1): 1246-125.
97. Wilson C, Koeberle M. CHAPTER 13. User-friendly Medicines. In., 2018; 343–85.
98. Shet N, Vaidya I, Banerjee N. Formulation and evaluation of aceclofenac sodium effervescent taste masked granules. Int J Bio Pharm., 2014; 5: 50 8.
99. Durfee S, Messina J, Khankari R. Fentanyl Effervescent Buccal Tablets. Am J Drug Deliv., 2006; 4(1): 1–5.
100. Vergeire DG, Usefulness of Cost Effectiveness: Evidence versus Applicability. Pharm Anal Acta., 2016; 7: 456.
101. Sinko P.J. Ionic Equilibria. In: Troy D., editor. Martin's Physical Pharmacy and Pharmaceutical Sciences. Lippincott Williams and Wilkins Philadelphia; New York, NY, USA., 2006; 161–185.
102. Wanczinski Ferrari BJ, Pelegrini BL, Bassi da Silva J, Neves Pereira OC, Miriam de Souza Lima M, Bruschi ML. Formulation and in vivo study of the solid effervescent system as a new strategy for oral glutamine delivery. J Drug Deliv Sci Technol., 2021; 63: 102516.
103. Ciriminna R, Meneguzzo F, Delisi R, Pagliaro M. Citric acid: Emerging applications of key biotechnology industrial product. Chem. Cent. J., 2017; 11: 22.
104. Mawlieh B, Kalita K, Jyoti Sahariah B, Talukdar A, Sharma BN. Design and evaluation of antiurolithiatic effervescent herbal tablets containing hydroalcoholic extract of Bryophyllumpinnatum. Bull Pharm Sci Assiut., 2023; 46(1): 1–11.
105. Wagner-Hattler L, Wyss K, Schoelkopf J, Huwyler J, Puchkov M. In vitro characterization and mouthfeel study of functionalized calcium carbonate in orally disintegrating tablets. Int. J. Pharm., 2017; 534: 50–59.
106. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Acalypha Fruticosa Extract Tablets Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. World Journal of Pharmaceutical Research., 2024; 13(8): 1073-1091.
107. Othman AM, Alburyhi MM, Al-Hadad GH. Captopril-Excipient Preformulation Studies for Mouth Dissolving Tablets Development. World Journal of Pharmaceutical Research, 2025; 14(10): 1398-1420.

108. Alburyhi MM, Yahya TAA, Saif AA, Noman MA. Formulation and Evaluation of Lornoxicam Microsponge-Based Gel as A Transdermal Drug Delivery Systems. World Journal of Pharmaceutical and Life Sciences, 2025; 11(5): 200-217.
109. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Ginger Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. World Journal of Pharmaceutical and Medical Research., 2025; 11(6): 400-415.
110. Alburyhi MM, Saif AA, Noman MA, Saif RM. The Importance of Stability Testing in Pharmaceutical Development of Ceftriaxone Implant Biodegradable Tablets. Matrix Science Pharma (MSP)., 2025; 9(2): 58-63.
111. Saif AA, Alburyhi MM, Noman MA, Abudunia A. Amoxicillin-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. European Journal of Pharmaceutical and Medical Research., 2025; 12(6): 530-562.
112. Alburyhi MM, Hamidaddin MA, Noman MA, Saif AA. Recent Innovations of Novel Drug Delivery Systems for Formulation, Development and Evaluation of Metronidazole Medicated Chewing Gum Tablets. European Journal of Biomedical and Pharmaceutical Sciences, 2025; 12(6): 353-370.
113. Alburyhi MM, Saif AA, Noman MA, Abudunia A, Yassin SH, Abdullah JH. Formulation, Development and Evaluation of Amoxicillin Fast Dissolving Tablets. World Journal of Pharmaceutical and Life Sciences., 2025; 11(7): 183-197.
114. Alburyhi MM, Mohamed YAS, Saif AA, Noman MA. Compatibility Studies with Pharmaceutical Excipients of Amlodipine for the Development of Novel Delivery Systems. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(11): 95-136.
115. Alburyhi MM, Saif AA, Noman MA, Al-Ghorafi MA. Comparative Study of Certain Commercially Available Brands of Paracetamol Tablets in Sana'a City, Yemen. European Journal of Pharmaceutical and Medical Research., 2018; 5(12): 36-42.
116. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Tribulus Terrestris Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. World Journal of Pharmaceutical Research., 2024; 13(7): 1264-1282.
117. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Pandanus Odoratissimus Extract Capsules Delivery System as an Advanced Phytotherapy

Approach for Hepatoprotective. European Journal of Pharmaceutical and Medical Research., 2024; 11(4): 06-13.

118. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Vera Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(4): 1408-1423.
119. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Curcuma Longa Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(6): 37-43.
120. Noman MA, Alburyhi MM, El-Shaibany A, Alwesabi NA. Formulation and Evaluation of Pandanus Odoratissimus L Extract for Treatment of Nocturnal Enuresis as Orodispersible Tablets Delivery System. World Journal of Pharmaceutical Research., 2024; 13(5): 56 -71.
121. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Dictyota Dichotoma Extract Medicinal Seaweed Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(4): 63-70.
122. Dong X, Zhang W, Wang X, Liu S, Liang J, Liufu C. A Novel Preparation Method for Effervescent Tablets of Xianganfang Containing Fresh Juice using a Semi-Solid Extrusion 3D Printer with Three Cartridge Holders. AAPS Pharm SciTech., 2022; 23(6): 193.
123. Zhai H, Jones DS, mccoy CP, Madi AM, Tian Y, Andrews GP. Gastroretentive extended-release floating granules prepared using a novel fluidized hot melt granulation (FHMG) technique. Mol. Pharm., 2014; 11: 3471– 3483.
124. Sun W. Development of Effervescent Tablets Containing Elderberry Vine Tea Compound and Evaluation of Their Antioxidant Activity. Zeb A, editor. J Food Process Preserv., 2023; 2023: 1–14.
125. Zheng X, Wu F, Hong Y, Shen L, Lin X, Feng Y. Improvements in sticking, hygroscopicity, and compactibility of effervescent systems by fluid-bed coating. RSC Adv., 2019; 9(54): 31594-608.
126. Julianti TB, Bakar MFA, Wikantyasning ER. Formulation and optimization of effervescent tablet containing Kaempferia galanga. Int J Appl Pharm., 2024; 15: 133–9.

127. Obara T, Prevalence, Determinants, and Reasons for the nonreporting of Adverse Drug Reactions by Pharmacists in the Miyagi and Hokkaido Regions of Japan, Advance Pharmacoepidemiology and Drug Safety., 2015; 4: 191.
128. Murdiana HE, Revika E, Rahmawati D, PuspitasariPutri AD, Murti BT. Moringa oleifera lam.- based effervescent tablets: Design, formulation and physicochemical evaluation. Int J Drug Deliv Technol., 2018; 8(4): 222–8.
129. Nurul SMS, Norhayati M, Nur Fazira AR. Phytochemical Contents and Antioxidant Properties of Polyherbal Effervescent tablets formulated with Different Effervescent Agents. Res J Chem Environ., 2022; 26(3): 1–7.
130. Machmud E. Effectiveness of Roselle Effervescent Tablets as Traditional Medicinal Plants in preventing Growth of Candida albicans Colonies and Streptococcus mutans. The Journal of Contemporary Dental Practice., 2018; 19(8): 925–8.
131. H Akg¨ul, F S Mohammed, E Kına, I Uysal, M Sevindik, M Dog˘an. Total Antioxidant and Oxidant Status and DPPH Free Radical Activity of Euphorbia Eriophora. Turkish Journal of Agriculture-Food Science and Technology., 2022; 10(2): 272–275.
132. H Chowdary, A Venkaiah, S Malik, H Reddy, S Achari, P Raju. Dissolution Test as a Quality Control Tool for Herbal Formulations-A Comprehensive Review. IJIPSR., 2014; 5: 364–369.
133. I Uysal, FS Mohammed, AES¸abik, E Kına, M Sevindik. Antioxidant and Oxidant Status of Medicinal Plant Echium Italicum Collected from Diferent Regions. Turkish Journal of Agriculture-Food Science and Technology., 2021; 9(10): 1902–1904.
134. E Kına, I Uysal, FS Mohammed, M Dogan, M Sevindik. In-vitro Antioxidant and Oxidant Properties of Centaurea Rigida. Turkish Journal of Agriculture-Food Science and Technology., 2012; 9(10): 1905–1907.
135. Y Hayaza, A RestiErwiyani, J Susilo. Formulasi Dan Pengaruh Konsentrasi Asam Sitrat, Asam Tartrat Dan Natrium Bikarbonat Terhadap Sifat Granul Efervescent Ekstrak Labu Kuning (Cucurbita Maxima Duch). Journal of Holistics and Health Sciences (JHHS)., 2019; 1: 11–19.
136. R Rowe, P Sheskey, M Quinn. Handbook of Pharmaceutical Excipients., 2009.
137. The United, NF 28 Convention Inc. USA: United States Pharmacopeia United States Pharmacopeial Convention., 2010.