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FORMULATION AND EVALUATION OF PARACETAMOL GUMMIES

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Abstract:

Gummies are a class of confections based on a hydrocolloid that provides a network to hold relatively high moisture content sugar syrup. The aim is to produce healthier and palatable gummy jellies that have improved nutritional characteristics and maintain their traditional textural characteristics. These developments align with consumer demands for healthier confectionery products and the need to protect public health.

Introduction:

Gummies are a class of confections based on a hydrocolloid that provides a network to hold relatively high moisture content sugar syrup. Traditionally, gelatine-based candies are referred to as gummies (also spelled as gummy). Gummies are the common name for candies manufactured using different hydrocolloids such as Gelatine, starch, and pectin are the three most prevalent hydrocolloids. Each hydrocolloid gives the candy a different texture and set of organoleptic qualities. Both adults and children frequently use gummies as a product. At least three times each week, these products are ingested by 86.8% of children between the ages of 6 and 8. Due to their organic and chewy nature, gummies are especially well-liked among those under the age of 17. They usually consist of jellifying agents (pectin, modified starch, gelatine, etc.) fruit, sugars, and colorant where water-soluble ingredients can be dissolved and the insoluble ones are suspended in the viscous matrix. Due to their appearance, flavor, and texture, and the fact that patients in pediatric and geriatric contexts have the highest compliance rates, gummies offer a wide range of applications in the pharmaceutical industry as a novel drug delivery technology. Gummies are more acceptable to children and certain adults. It is regarded as the most practical and secure way to distribute medications. To produce gummies, the use of natural juices or purees of oranges, strawberries, and other fruits, or even fruit by-products, has been studied. These can develop healthier formulations with antioxidant capabilities in addition to enhancing the organoleptic features of gummies.

Jellies and gummies are popular with both children and adults. The base of a gummy bear is typically composed of a jellifying agent (pectin, modified starch, gelatin, etc.) and sugars, in which water-soluble ingredients can be dissolved and insoluble ingredients are suspended in the viscous matrix. As a result, the application range of gummies is broad.

According to EMA guidelines, liquid formulations are best suited for patients under the age of eight. Nevertheless, due to their solubility, the dose of bio-actives in liquid goods is restricted, and several additives, such as sweeteners, buffers, preservatives, and so on, must be added to assure physical, chemical, and microbiological stability and improve flavor. Gummy bears made from natural materials with active compounds are a more complex formulation strategy. Gummy bears, like all other chewable food products, are exclusively available to children and adults.

The pharmaceutical and food industries see it as a novel drug delivery system that is more appealing to children and some adults due to its confectionary appearance and taste. However, excessive consumption of these products can have negative impacts on public health due to their high sugar and additive contents, as well as the presence of undesirable compounds generated by the heat treatment. To address these concerns, there is increasing pressure on the industry to reduce sugar in these products and explore healthier alternatives. One possible alternative is to reduce or replace sugars with other sweetening products such as honey. Natural juices or purees of fruits, particularly those with high amounts of antioxidants, are also being considered as healthier options for manufacturing jellies and gummies. Additionally, the use of anthocyanin extracts can provide an alternative to synthetic colorants and have additional beneficial health effects.

Research groups are actively developing alternative formulations of gummy jellies that contain natural ingredients without any additional sugar or synthetic food additives, such as orange juice and red fruit puree. These formulations are being evaluated in terms of color, texture, antioxidant activity, microbiologic safety, nutritional composition, and sensorial evaluation to demonstrate their health benefits while preserving most of the desirable organoleptic properties of traditional gummies and jellies.

Natural juices or purees of orange, strawberry, and other red fruits, as well as fruit by-products, have been considered for use in the production of jellies.

Not only can these improve the organoleptic properties (color, flavor, and texture) of gummies and jellies, but they can also produce healthier formulations with antioxidant properties Recent studies have shown that adding anthocyanin extracts to gelatin and pectin gels can not only provide an alternative to synthetic colorants but also have additional health benefits for those who consume the products in moderation.

Some of the research groups are also formulating the formulation of multivitamin gummies. The first Recommended Dietary Allowances (RDAs) for vitamins and minerals were established in 1941, and since then, more vitamins and minerals have been added to the list. Currently, calcium, iron, and vitamins A, B1, B2, and C. 1968 Magnesium, vitamins E, B6, and B12, and others are later added to the list. moment Vitamins A, B1(thiamine), B2 (riboflavin), B3 (niacin), B5(pantothenic acid), B6(pyridoxine), B7(biotin), B9(folic acid), B12(cobalamin), C, D, E, K, choline, calcium, chromium, bobby , iodine, iron, magnesium, manganese, molybdenum, phosphorus, selenium, zinc, potassium, and chloride that are considered essential for maintaining good health.

Riboflavin has boosted energy levels, improved vulnerable system activities, and promoted healthy hair, skin, and nails. It promotes hair growth by increasing vitamin B6 and niacin levels.

A higher carbohydrate content causes a greater response to blood glucose levels, known as available carbohydrate.

Aside from available carbohydrates, there are numerous other food factors that can affect GI and GL values, one of which is the food's gelling properties. Because of the versatility of hydrocolloids in forming specific dosage forms, gummies' chewiness and swallow ability has made them popular among consumers Because of their thickening and gelling properties, hydrocolloids used in gummies can slow down mixing and mass transfer processes and alter the flavor or nutrient release by increasing the viscosity of gastrointestinal fluids in the stomach or small intestine.

Ordinary gummies contain large amounts of sweeteners such as sucrose, glucose syrup, gelatin, and seasoning, which is critical for consumer acceptance due to their sweetening ability and influence on the product's texture. Because of its high glycaemic index, sucrose is the most often used sweetener, however, it has increasingly been supplanted by artificial sweeteners. Maltitol and erythritol are regarded as good substitutes not just for their pure sweetness, but also for their restricted hydrolysis by the human enzyme system, which has no influence on glucose metabolism.

Gummy vitamins effectively improve the texture of the skin, hair, and nails. These gummies can indeed help to ameliorate energy situations and perform day-to-day tasks with complete energy.

Gummies can also be made from fruits like Watermelon and beetroot contain various nutrients and bioactive compounds that can provide health benefits. For example, watermelon is a good source of lycopene, an antioxidant that has been shown to reduce the risk of certain types of cancer and improve cardiovascular health. Beetroot is high in dietary nitrates, which can lower blood pressure and improve exercise performance.

By incorporating these ingredients into gummies, they can become a fun and tasty way to enjoy the health benefits of watermelon and beetroot. It is important to note that while gummies can be a healthy snack option, they should be consumed in moderation as they can also contain added sugars and calories.

Gummy vitamins are designed to be more palatable and easier to consume than traditional vitamin tablets and capsules. They come in a variety of flavors and are easy to chew and swallow. They are also less likely to cause stomach discomfort than traditional tablets and capsules. Gummy vitamins can be a convenient and delicious way to supplement one's diet with essential vitamins and minerals. However, it is important to remember that they should not be used as a substitute for a healthy and balanced diet

The aim is to produce healthier and palatable gummy jellies that have improved nutritional characteristics and maintain their traditional textural characteristics. These developments align with consumer demands for healthier confectionery products and the need to protect public health.

Paracetamol acts as an Analgesic (pain reliever), Anti-inflammatory (swelling reducer), and Antipyretic (fever reducer) drug with few interactions with other pharmaceuticals. Scientists do know that paracetamol, or acetaminophen, acts on the brain to inhibit prostaglandin production.

ANALGESIC

Paracetamol is a popular analgesic agent used to manage both acute and chronic pain. However, its metabolism is complicated, and its analgesic processes remain unknown. Previously, it was believed that acetaminophen caused analgesia by inhibiting cyclooxygenase enzymes; however, it has recently been proposed that ac Paracetamol's main analgesic mechanism is its metabolization to N-acylphenolamine (AM404), which then acts on the transient receptor potential vanilloid 1 (TRPV1) and cannabinoid 1 receptors in the brain. It has been discovered that the Paracetamol metabolite AM404 causes analgesia directly via TRPV1 receptors on C-fiber endings in the spinal dorsal horn. It is known that similar to the brain, the spinal dorsal horn is crucial for pain pathways and modulates nociceptive transmission. As a result, Paracetamol causes analgesia by working on both the brain and the spinal cord. Furthermore, due to its weak inhibition of cyclooxygenase, Paracetamol is not thought to have any anti-inflammatory action. (COX). However, in an inflammatory pain rat model, AM404 generates analgesia via TRPV1 receptors on the spinal dorsal horn, and these analgesic effects were stronger in the model than in naive rats. The goal of this review was to summarize previous and novel problems concerning Paracetamol's analgesic mechanisms. It will enable clinicians to explore new Paracetamol based pain management techniques.

Analgesic Mechanism of Paracetamol

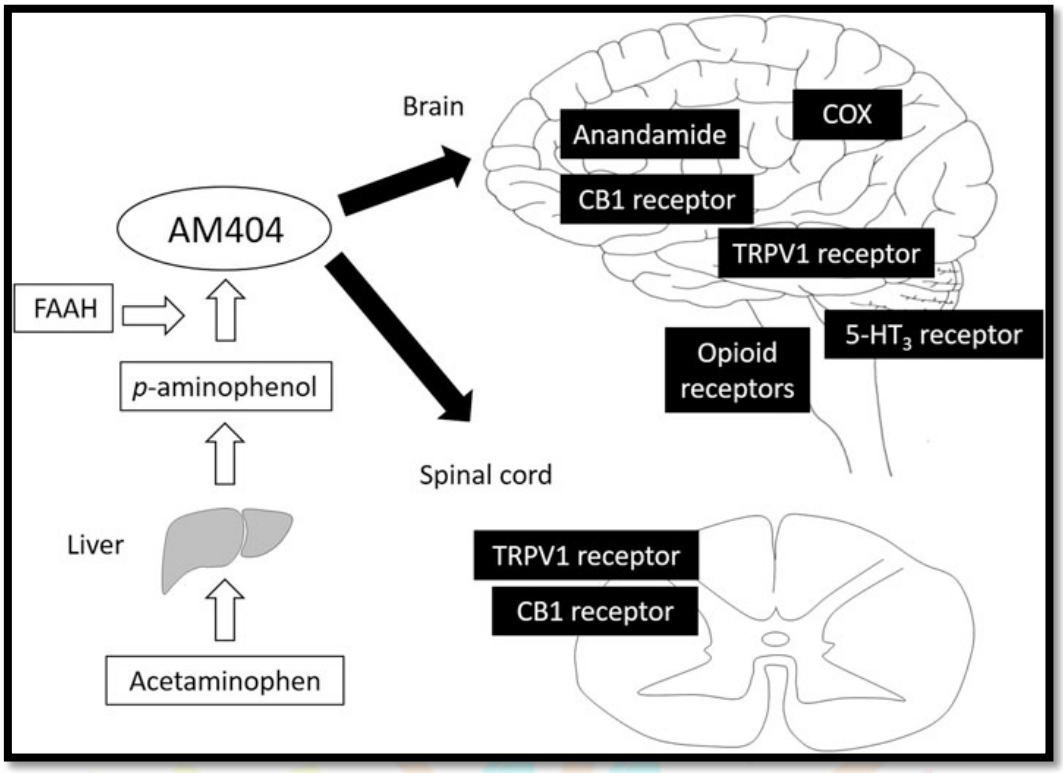
Inhibition of CO-X Activity:

It has been thought that Paracetamol induces analgesia by inhibiting the enzymes COX-1 and -2, which produce prostaglandins from arachidonic acid. Unlike NSAIDs, however, Paracetamol interferes with the peroxidase activity of COX isoenzymes, primarily COX-2, with little therapeutic effect and is highly dependent on the state of environmental oxidation (1,2).

It has also been reported that the third COX isoenzyme, COX-3, a COX-1 exon splice variant, is particularly sensitive to Paracetamol.(2)

However, COX-3 was quickly discovered to be absent in humans, and subsequent research indicates that Paracetamol has no clinically significant impacts on the COX-1 exon splice variants discovered in humans thus far.(3)

The suppression of COX activity is no longer thought to be the primary analgesic mechanism of Paracetamol.



Other Mechanism:

Another possible reason for the analgesic action of acetaminophen could be the action of endogenous neurotransmitter systems including opioid and serotonergic systems. Many studies have found that acetaminophen's analgesic effect includes the activation of endogenous opioid pathways, which leads to analgesic spinal-supraspinal self-synergy.(4)

Acetaminophen works not only on the brain but also on the spinal cord and induces analgesia. Furthermore, the most likely analgesic mechanism is that the acetaminophen metabolite AM404 works by activating TRPV1 and/or CB1 receptors. Findings also support a mechanism by which acetaminophen causes analgesia in inflammatory pain conditions. The findings are applicable to clinical pain management with acetaminophen, but the analgesic mechanism of acetaminophen has not been fully elucidated. Therefore, further discussions and studies will be needed to understand the action of acetaminophen. (5)

ANTI-INFLAMMATORY

An anti-inflammatory is a substance or medication that helps to reduce inflammation in the body. Inflammation is a localized response (reaction) of vascularized, living tissues to exogenous and endogenous stimuli. The word translates from the Latin word "inflammare," which means to burn. Essentially, inflammation acts to localize and eliminate the underlying cause of tissue injury in addition to serving to control tissue damage. Thus, inflammation is a normal (protective) reaction to harm. It is best to think of inflammation as a helpful response to either violence or certain illnesses rather than as a disease in and of itself.

The common signs of inflammation, such as redness, discomfort, swelling, and heat, have been recognized by mankind for hundreds of years. Several diseases, including those with large global prevalence like rheumatoid arthritis, atherosclerosis, and asthma, are impacted by inflammation.

One class of anti-inflammatory medications is non-steroidal anti-inflammatory drugs (NSAIDs), which include aspirin, ibuprofen, and naproxen. These medications work by inhibiting the production of prostaglandins, which are chemicals that promote inflammation. While NSAIDs can be effective in reducing inflammation and pain, they can also have side effects, such as gastrointestinal bleeding and kidney damage.

Another class of anti-inflammatory medications is corticosteroids, which are more powerful than NSAIDs and are typically used to treat more severe forms of inflammation, such as autoimmune disorders. By reducing the immune system's response to inflammation, corticosteroids work. However, they can also have side effects, such as weight gain, mood changes, and increased risk of infections. (6,7)

Mechanism of Action

Anti-inflammatory medications work by reducing inflammation in the body, which is a natural response to injury or infection. Inflammation is a complex process that involves a variety of chemical mediators, including prostaglandins, leukotrienes, and cytokines. These mediators are produced by immune cells in response to tissue damage or infection and they promote the recruitment of more immune cells to the site of injury or infection.

Non-steroidal anti-inflammatory drugs (NSAIDs) work by inhibiting the production of prostaglandins, which are important mediators of inflammation. Prostaglandins are produced by an enzyme called cyclooxygenase (COX), and NSAIDs block the activity of COX, thereby reducing the production of prostaglandins. This leads to a reduction in inflammation, pain, and fever. (8)

ANTIPYRETIC (8)

Fever is one of the most common clinical symptoms managed by pediatricians and other health care providers and accounts, by some estimates, for one-third of all presenting conditions in children. Fever in a child commonly leads to unscheduled physician visits, telephone calls by parents to their child's physician for advice on fever control, and the wide use of over-the-counter antipyretics.

The usage of antipyretics is not well understood, even though their complicated biochemistry is becoming increasingly clear. Although doctors, nurses, pharmacists, and parents frequently use antipyretics, it is still unclear whether lowering a patient's core temperature is beneficial for those who are febrile. Fever plays a crucial part in the host's defense in animal models of infection, and pyrexia may have positive effects on illness, as has been discussed elsewhere. (9)

Physiology of Fever

It is important to underline that fever is not a sickness but rather a physiological function that helps the body fight infection. Fever increases the generation of neutrophils and T lymphocytes, inhibits the growth and reproduction of germs and viruses, and supports the body's acute-phase response. Fever intensity does not necessarily correspond to sickness severity. Most fevers are benign, short-lived, and may even serve to protect the host. Although fever can make kids uncomfortable, research suggests that it has positive impacts on some immune system components and that it speeds up the body's recovery from viral illnesses. It is unclear if using antipyretics, especially ibuprofen alone or in conjunction with acetaminophen, increases the risk of complications from some infections. Relief from patient discomfort and a decrease in inadvertent water loss are two potential advantages of fever lowering, both of which may help to prevent dehydration. The risks of decreasing fever include drug toxicity and a delay in making the correct diagnosis and starting the proper course of therapy. There is no proof that children with fever, as opposed to those who are overheated, are more likely to have negative consequences such brain as damage. In reaction to endogenous and external pyrogens, the hypothalamic "set point" rises, which is a frequent and normal physiological response known as fever. Contrarily, hyperthermia is a rare pathophysiologic response that causes more heat to be produced than can be dissipated due to failure of normal homeostasis (no change in the hypothalamic set point). Hot, dry skin and central nervous system failure that causes delirium, convulsions, or coma are features of hyperthermia. As soon as hyperthermia is detected, it should be treated since harmful physiologic effects start to manifest at temperatures exceeding 41 to 42°C. Surveys of healthcare professionals, including doctors, have shown that the majority hold the incorrect idea that temperatures exceeding 40°C (104°F) increase the risk of heat-related poor consequences. A youngster with a temperature of 40 °C (104 °F) who has a simple febrile sickness is completely different from a child

who has a temperature of 40 °C (104 °F) who has suffered from heat stroke. It is therefore difficult to extrapolate similar results from these various conditions.(10)

POLYMER

The term polymer is generally used to indicate many high molecular weight substances, which are found in many forms and numbers due to the presence of very large numbers and types of atoms in their molecules. Polymers exhibit different chemical structures, physical properties, mechanical behavior, thermal characteristics, etc., based on which they are classified in different ways.

Gelling Agents

Pectin (11)

Pectin is a polysaccharide from plant sources and it is commercially obtained from citrus (orange peel and lemons) and pomaceous (apple) fruits by using acid (hydrochloric) at pH 2.0 and is mainly used in jam, confectionery and candy production (Labropoulos & Anestis, 2012; Lees & Jackson, E., 1973). The difference between citrus pectin and apple pectin is the color of the product. Citrus pectin has a more brown color than apple pectin and this limits its use in confectionery (Lees & Jackson, E., 1973). In gel formation, the amount of pectin, the solution temperature, the pH of the solution and the sugar concentration are significant. Low pH (up to 3.2) provides firm gels however, below this pH the desired firmness cannot be formed since carboxylic acids groups on the pectin back bone needs to be protonated to provide crosslinking through H-bonding. The gel strength of pectin is described as the sugar amount (gram) that produces a standard gel texture with one-gram pectin. In candy production, the gel strength of pectin is 150 (Lees & Jackson, E., 1973).

Starch (11)

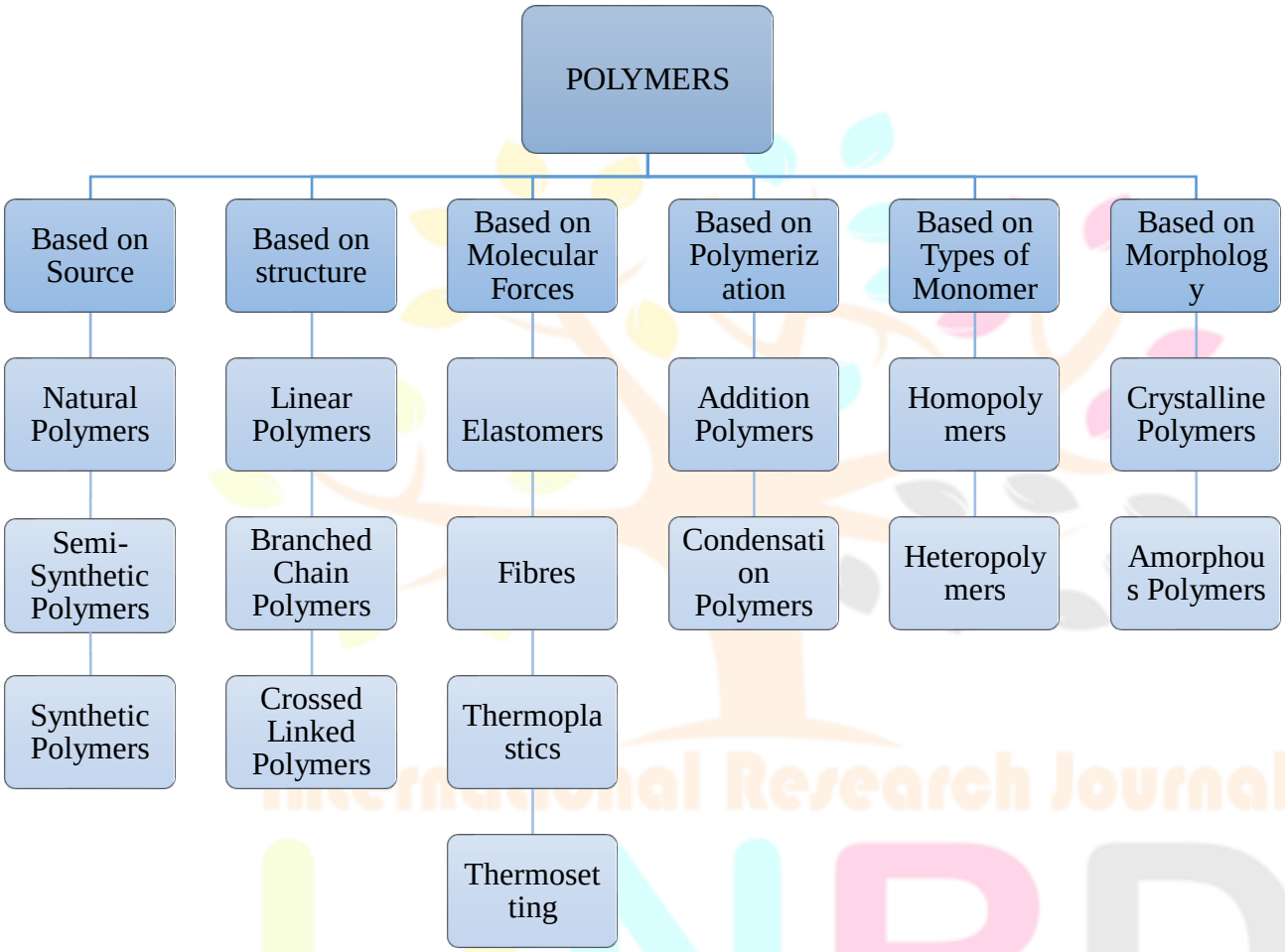
Starch is the reserve tissue of the many types of plants. In human diet, starch provides 70-80% of carbohydrates (Labropoulos & Anestis, 2012). Starch has white, odorless, and powder structure and it is produced from many sources such as, potato, rice and corn whose physical and chemical properties differs from each other (Lees & Jackson, E., 1973). In sugar confectionery, mainly corn starch is used as a gelation agent, and coating agent due to its reliability, better textural properties and production efficiency (Lees & Jackson, E., 1973). Starch has two components, namely, amylose (linear-chain) and amylopectin (branched-chain) (Labropoulos & Anestis, 2012). The concentrations of these vary according to the plant source (Lees & Jackson, E., 1973). Yet, starch includes 20-30% amylose and 70-80% amylopectin, in general (Labropoulos & Anestis, 2012). When a starch solution is heated and temperature reaches to a certain point, starch gelatinization, which is specific for the type of the starch, occurs. The gelatinization temperature differs according to the source of the starch and this gelatinization establishes enhancement of viscosity and solubilization (Labropoulos & Anestis, 2012). Starch is insoluble in cold water yet the viscosity increases with the increasing temperature (Labropoulos & Anestis, 2012). The native starch has some limitations in food industry, such as, retrogradation (Ashogbon & Akintayo, 2014). In order overcome these drawbacks, the starch is modified in diverse forms such as, thin boiling starch and oxidized starch which are mostly used in confectionery (Labropoulos & Anestis, 2012; Lees & Jackson, E., 1973). A thin boiling starch has a better firmness than native starch and oxidized starch has a better stability than unmodified starch (Lees & Jackson, E., 1973). As an example, for Turkish delight production modified starch is used mostly.

Gelatin (Bovine) (12)

Gelatin is composed of 85-92% proteins and the remaining are minerals, salts, and water. Collagen, in animals (from cattle hide, pigskin) and human tissues, is partially hydrolyzed to obtain gelatin (Schrieber & Gareis, 2007). Moreover,

15gelatin includes all essential amino acids except tryptophan. It is known that, 10 g of gelatin has the same amount of glycine as 160 g meat (Schrieber & Gareis, 2007). There are two types of gelatin with respect to the different isoelectric points: acid conditioned type A and alkaline-conditioned high-Bloom type B (Schrieber & Gareis, 2007). Gel strength (gelling power) is the most crucial parameter to describe gelatin, which is determined by Bloom test. Bloom test measures gel firmness of 6.67% gelatin which is aged for 17h at 10 °C as a function of time and the absolute value is shown as grams (Schrieber & Gareis, 2007). Bloom values have the range of 50-300 and owing to this, three types of gelatin arise that are namely, high-Bloom (200-300), medium-Bloom (100-200) and low-Bloom (50-100). High-Bloom gelatin has higher melting point, shorter time of gelation, more neutral taste, lighter color, and stronger gel strength. Schematic of the gelation for gelatin mechanism is given in Figure 1.8. In gelatin-based gels the gelation is reversible (thermoreversible) (Schrieber & Gareis, 2007). Gelatin has many different characteristics such as, texturizing, foaming, stabilization, thickening, water binding and most importantly an excellent gelling agent. This why, gelatin is so popular and used in different various industries including pharmaceutical, paper processing and food. In confectionery, gelatin is mainly used in fruit jellies since due to melting point at the body temperature by absorbing water quickly it results in the release of flavor. The physical properties of gelling agents are shown in Table 1.2 (Schrieber & Gareis, 2007).

Classification of Polymers



LITERATURE REVIEW: PARACETAMOL

ACTIVE PHARMACEUTICAL INGREDIENT	TYPE	LITREATURE
Paracetamol	Oro-dispersible, fast-disintegrating paracetamol tablets. (13)	Ceschi A, Hofer KE, Rauber-Lüthy C, Kupferschmidt H. Paracetamol oro-dispersible tablets: a risk for severe poisoning in children?. European journal of clinical pharmacology. 2011 Jan;67:97-9.
	Gummy candies (14)	Chabib L, Murrukmihadi M, Aprianto A. Pengaruh Pemberian Variasi Campuran Sorbitol Dan Glukosa Cair Sebagai Pemanis Pada Sediaan Gummy Candy Parasetamol. Jurnal Ilmiah Farmasi. 2013 Aug 5;10(2):69-77.
	Vegan, sugar-free gummy candies (15)	Gouveia TI. Development of vegan, sugar-free gummy candies-applicability to formulations with paracetamol.
	Soft-Chewable Paracetamol Tablets (16)	Sabere AS, Suhaimi NA, Ahmed QU, Mahat MM, Roslan NC, Azizi J. Soft-chewable paracetamol tablets by melt granulation method: Formulation and characterization. Journal of Pharmacy & Bioallied Sciences. 2021 Jul;13(3):312.

LITERATURE REVIEW

Development and characterization of healthy gummy jellies containing natural fruits (28)

(Edite Teixeira-Lemos, *et.al.)*

Gummy jellies, which often lack any health benefits, now have some thanks to the reduction of sugar and addition of substances that promote wellness the nourishment. The objective of this study is to create two types of gummy jellies with natural components, no sugar or additives added, one with orange juice and mildly sweetened with honey (ORH), and the other with puree created from a variety of berries (BEM). They were subjected to analyses using sensory, microbiological, and physicochemical methods. Microbiological testing revealed that both gummies were safe for ingestion in accordance with EU

regulations. A nutritional assessment was made possible by the physical-chemical studies, and ORH and BEM presented 73.8 kcal/100 g and 39.8 kcal/100 g, five and nine times less than comparable commercial items, respectively. The following are the macronutrient contributions of ORH and BEM: 78.0 and 67% of energy comes from carbohydrates, whereas 21.7 and 33% come from proteins. The antioxidant capacity for ORH and BEM, respectively, was 50.4 4.5 mg/L TE and 83.7 7.6 mg/L, respectively, in terms of possible functional characteristics. Sensory analysis revealed that although the produced gummy jellies were significantly less liked than their commercial counterparts, panellists liked them nonetheless, especially the ORH, which received ratings that were practically on par with those of the commercial sample. The created gummies also displayed increased antioxidant capacity and lower calorie values.

Red beet extract usage in gelatin/gellan-based gummy candy formulation introducing Salix aegyptiaca distillate as a flavoring agent. (29)

Ehsan Moghaddas Kia, *et.al.*

The functionalization of food products with all-natural, health-improving ingredients is very popular today. Red beets naturally contain betalains, which are well known for their health-improving properties. The purpose of this study was to evaluate gummy sweets made using gellan gum (0.5 or 1.5%) as the gelling co-agent and red beetroot extract (0.1 or 0.3%) as the coloring and flavoring agents. The created gummy candy samples underwent sensory evaluation, texture profile analysis, DPPH assay, and color analysis. With an increase in gellan gum content in the gummy candy formulation, the results showed that hardness (60 N) improved and gumminess (15 N) reduced. By adding red beetroot extract, the samples' ability to scavenge free radicals increased (by 50%) significantly, according to statistical analysis (p 0.05). Furthermore, when compared to gummy candies made of gelatin, samples made with gellan gum were lighter and produced a glossy red color. The judges who discussed sensory evaluation agreed that adding Salix aegyptiaca to the gummy candy enhanced its sensory qualities (overall acceptance from 7.4 to 8.2; out of 9). According to our research, the food industry has a huge potential for the use of red beetroot extract as an acid-stabilized natural color, gellan gum (a highly transparent, acid-resistant, gel-forming gum), and Salix aegyptiaca distillate as a structuring, coloring, and flavoring agent, respectively.

Physicochemical, textural, and sensory qualities of pectin/gelatin gummy jelly incorporated with Garcinia atroviridis and its consumer acceptability (30)

Gerry Renaldi, *et.al.*

The purpose of this study was to create a gummy jelly product using a purée of Garcinia atroviridis fruit, pectin from the fruit's rind, and gelatin from Salmo salar skin, and to examine its impact on the product's physicochemical properties, texture, and sensory qualities, as well as its acceptability among consumers. By adjusting the amounts of pectin (0.5-1.5%) and gelatin (8.5-9.5%), the formulation of gummy jelly was optimized using the mixture design method. Pectin (1.42%) and gelatin (8.58%) were the main ingredients in the G. atroviridis gummy jelly's (GAGJ) optimized formulation. Consumer acceptance of the GAGJ produced by the optimized formula demonstrated a moderate sensory rating score (6.9–7.5) and showed no correlation between Muslim and non-Muslim consumers' acceptance and purchase decisions, whereas consumers' age and occupation had a significant impact on the consumers' acceptance and purchase choices. A product containing significant bioactive components and antioxidant properties, such as GAGJ's DPPH (0.29-0.30 mg ascorbic acid equivalent (AAE)/g dried sample), ABTS (0.45-0.47 mg AAE/g dried sample), and FRAP (0.39-0.41 mg AAE/g dried sample), which have been shown to have positive effects on health.

Effect of gelatin content and oral processing ability on vitamin C release in gummy jelly. (31)

Xing-yu Zhou, *et.al.*

Four levels of gelatin (3%, 6%, 9%, and 12%) were chosen for the investigation into the variables influencing the release of vitamin C (VC) in gummy jelly during oral processing. Chewing tests were performed using a bionic chewing robot. When the gelatin percentage was increased from 3 to 12%, textural profile research revealed that the hardness of gummy jelly increased from 91.7 N to 198.8 N. VC release was positively connected with chewing frequency (Fchew) and chewing strain (STchew), but negatively correlated with gelatin content, chewing speed (SPchew), and saliva volume, according to a single factor chewing experiment (Vsaliva). An orthogonal chewing experiment revealed that the following elements were altered by VC release in order of importance:

STchew > Fchew > SPchew > Vsaliva.

A model to forecast the volume of VC released was proposed using multivariate linear regression analysis, and the model's goodness-of-fit was 95.7%. The combination of Fchew 12 times, STchew 100%, Vsaliva 2 ml, and SPchew 40 times/min resulted in the largest amount of VC released. The ideal addition of gelatin was 6%. This study offered a useful guide for formula design and gummy jelly chewing mode optimisation.

Preparation and evaluation of gelatin and pectin-based Moringa oleifera chewable-gummy tablets (32)

Karina Citra Rani, *et.al.*

The ingredients in chewable gummy tablets are sugar and a gelling agent. As Moringa oleifera leaf powder has a high concentration of antioxidants and minerals, adding it to this dosage form has health benefits. This research created chewable gummy pills with moringa.Leaf powder produced with three different concentrations of each of two types of gelling agents.Pectin was created in concentrations of 1.0%, 1.5%, and 2.0%, whilst gelatin was made in 5.0%, 7.5%, and 10.0%. The objective of this study was to examine the effects of the type and concentration of the gelling agent on the physical properties of the manufactured chewable gummy tablets, including visual appearances, weight variation, tablet dimension, swelling ratio, dispersion time, syneresis, and texture profile (hardness, chewiness, and gumminess).After heating and congealing the chewable gummy pills, their physical features were examined using a completely random design (p0.05). The outcomes demonstrated that the nature and concentration of the dispersion time, syneresis, hardness, gumminess, and chewiness were all significantly impacted by the gelling agent and their interaction (p 0.05) as well as by the two independent variables. Because they meet all the physical characteristic requirements, exhibit no syneresis, and have the nicest texture among the created formulations, chewable gummy tablets made with 10% gelatin and 1.5% pectin are regarded as the best option.

A comparison of physicochemical properties of high drug-loaded tablets formulated with cold gelatin gummies (33)

N.D. Nnamani, *et.al.* Stress factors during dosage form formulation alter the parameters of drug release. The goal of this project is to create high drug-load tablets using the least amount of heat and water possible. The active pharmaceutical ingredients (APIs) used in this study are paracetamol and calcium carbonate powders, which have various thermal and solubility characteristics. High drug-loaded tablets are created using a combination of nanoprocessing and cold conditions. A 3:1 v/v acetic acid: water co-solvent solution was used to create a 25.0% weight-per-volume gelatin dispersion. The dispersion was heated to 112 °C for 30 minutes while being agitated, creating a gummy foundation that was then allowed to cool. Cold gummies with bases of 2.5, 5.0, 7.5, and 10.0% w/w in API were combined in two sets.Fourier transform infrared spectroscopy (FT-IR) and differential scanning calorimetry were used to assess the blends after they had been microwave dried (DSC). The mixtures were ground into granules, tested, and tabled. The pills' physicochemical characteristics were assessed. Three group test analysis of covariance was used to analyse the data. The mixes' FT-IR readings revealed no incompatibility. The semi-crystalline and amorphous solidifications of paracetamol and calcium carbonate dispersions, respectively, were shown by the DSC thermographs. The paracetamol granules showed 9.52% Carrs' indices and 1.11 Hausner ratios.The Carrs' indices and Hausner ratios of the calcium carbonate granules were 20.00–34.38 and 1.25–1.52, respectively. In contrast to the calcium carbonate tablets, which had tensile strengths of 2.53 to 5.09 MPa and D40s of 70.11 to 75.75%, the paracetamol tablet had a tensile strength of > 3.83 MPa and achieved total dissolution after 40 min. Cold gelatin gummies had no discernible impact on the qualities of high drug-load granules (p> 0.05), although they did have an impact on tablet dissolving (p> 0.05). The cohesiveness, crushing strength, and dissolution qualities of high drug-load tablets with low amounts of cold gelatin gummies were enhanced more for low thermal energy and fairly soluble paracetamol than for high thermal energy and poorly soluble calcium carbonate.

Effect of gelatin sucrose/glucose syrup ratio and citric acid on physical properties and sensory quality of gummy jelly product (34)

S Meesang, *et.al.*

The influence of gelatin, the ratio of sucrose to glucose syrup, and citric acid on the viscosity, hardness, cohesiveness, springiness, chewiness, gumminess, adhesiveness, overall acceptability, sweetness, and sourness of gummy jelly

product was studied using the response surface methodology. According to the findings, the empirical models for viscosity, hardness, cohesiveness, chewiness, gumminess, and chewiness (sensory quality) were significant (P 0.05) with R2 > 0.8. With an increase in gelatin content, the viscosity, hardness, cohesiveness, chewiness, and gumminess all increased. Viscosity, hardness, and chewiness were slightly reduced as the sucrose/glucose syrup ratio and citric acid level were increased. When 7% gelatin and 3.5% citric acid (in a 50% solution) were combined, the chewiness acceptability score was highest.

Improvement of vitamin C stability in vitamin gummies by encapsulation in casein gel (35)

Bing Yan, *et.al.*

The simplicity of ingesting, appealing look, and delectable tastes of vitamin gummies have helped them become more well-liked in recent years. When exposed to oxygen, moisture, light, heat, and changes in pH throughout production and shelf life, water-soluble vitamins like vitamin C are vulnerable to deterioration. Consequently, enhancing vitamin stability and postponing the breakdown process are crucial. In this work, vitamin C was microencapsulated inside casein gel, then dried using a spray dryer to create vitamin C capsules that are known as "micro cheese powder" (MCP). The results of the Fourier transform infrared spectroscopy demonstrated a rise in the hydrogen bonding between vitamin C and casein as well as vitamin C and the gummy. In addition, the physical interaction between micellar casein, rennet-treated casein, and vitamin C was investigated using a quartz crystal microbalance with dissipation technology. Storage testing revealed that whereas unencapsulated vitamin C in the gummy only preserved 79% of its vitamin C under accelerated tests over a ten-week period, microcapsules incorporated into the candy retained 92% of its vitamin C. Encapsulated vitamin C in the gummy also shown greater vitamin C and colour retention at various temperatures, humidity levels, and lighting conditions as compared to the gummy's unencapsulated vitamin C.Vitamin C was protected from gummy in the simulated gastric fluid (SGF) and simulated intestinal fluid by MCP, which demonstrated a decreased rate of release (SIF). Water-soluble vitamins in gummies may be more stable during processing and storage thanks to the new vitamin C microencapsulation.

Formulation and Evaluation of Multivitamin Gummies. (36)

Rutuja R. Khatode, *et.al.*

A multivitamin is a prescription drug that contains vitamins, beneficial minerals, and other nutritional building blocks as a preventative supplement. Vitamins C, B2, Zinc, Calcium, Magnesium, and Potassium are included in multivitamin formula. Gummy vitamins are intended to be more pleasant than ordinary vitamins (read: sweeter).People will be more likely to use them in the expedients. Although sticky vitamins have goopy flavours and a delicate taste, many individuals prefer them to capsules. Vitamins that are soluble, chewable, sticky, or greasepaint tend to be easier to digest. Vitamins are provided via gummies, much like in capsules and capsules.Vitamin C and Vitamin B2 (riboflavin) are the most important vitamins in multivitamin gummies since they both have powerful antioxidant effects, promote hair development, and treat eye-related disorders.Independent effects of activity and migraine on healthy skin and hair. In the body, citric acid has protective properties. It can kill bacteria, reduce urine acidity, and is utilised in sticky situations. Agar is frequently used to gel, thicken, stabilise, and adjust density for gummies. Gummies are enhanced with pure honey, which adds to their mouthwatering flavour. Orange juice displays antioxidant activity and provides sticky a great flavour.

Development of fiber rich gummies. (37)

Priya Bharat Lohar, *et.al.*

The demand from consumers for functional foods and nutraceuticals has grown across the globe in recent years.The trend is moving towards natural colourants, reduced fat, and low Cholesterol, natural elements derived from nature, and no artificial additions.With fewer restrictions than other dose forms, gummy food supplements are more widely accepted.As fibre helps with healthy digestion, gut macrobiotic composition, cholesterol reduction, and cardiovascular health, it is a crucial ingredient in the average diet. According to research, consumers are more inclined to turn to fibre as a value-added component for a healthy lifestyle.Our study's objective was to create fiber-rich gummies. Watermelon juice, beet juice, plant-based pectin in place of gelatin, and stevia are the main ingredients.

According to the current study, the product is a good source of carbs (64.52%) and dietary fibre (8.54%). All the participants really enjoyed the product (score- 8.) The nutritional value of gummies was calculated using a number of proximate analyses. Even sensory and microbiological analyses were carried out to determine consumer preference and safety, respectively.

PROFILES

PARACETAMOL PROFILE

Drug Description

Introduction:
Paracetamol was first synthesized in 1878 by Morse, and made available for medicinal use in 1883. However, because of a misinterpretation of its safety profile, it was only briefly used until the 1950s, when renal toxicity forced the withdrawal of the chemically related and previously favored analgesic, phenacetin. With accessibility over-the-counter, use across almost all age groups, and place at Step 1 of the WHO analgesic scale, paracetamol is undoubtedly the most widely used medication in the world today.

Name:
Paracetamol

Synonyms:
Acetaminofen, Paracetamol, Paracetamolo, and Paracetanol

Chemical Formula:
C8H9NO2

IUPAC Name:
4- Hydroxy acetanilide

Average Molecular Weight:
151.2 g/mol

Structure:

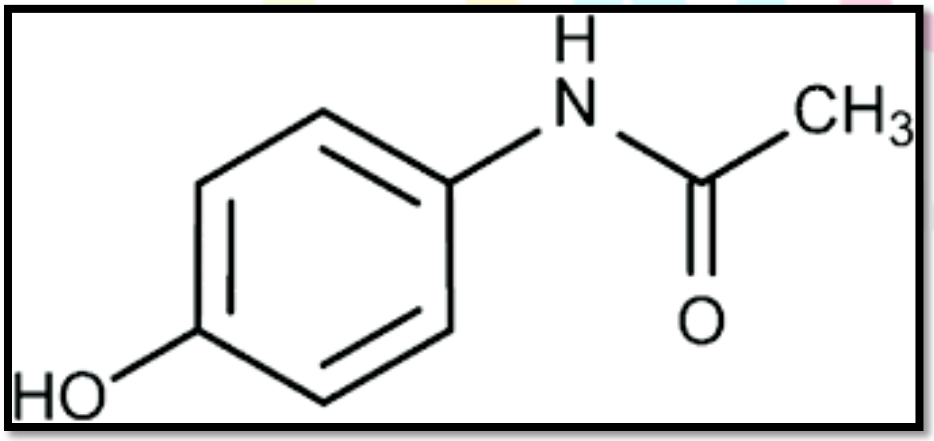


FIG. NO. 01: STUCTURE OF PARACETAMOL

Other Characteristics:

It is white, crystalline powder, sparingly soluble in water, freely soluble in alcohol, very slightly soluble in ether, and in methylene chloride.

Available Products available in the Market

Generic Name	Dose	Dosage Form	Brand Names	Manufacturer
Paracetamol	500mg	Tablets	Panadol	GSK
	500mg	Tablets	Pedrol	Stanley
	120mg/5ml	Suspension	Samophen	Adamjee
	500mg	Tablets	Febrol	Barrett Hodgson
	150mg/ml	Injection	Fevenor	Global Pharmaceuticals

Indications:

Paracetamol is one of the most commonly used **'over-the-counter'** analgesic for:-

- Headache
- Mild Migraine
- Musculoskeletal pain
- Dysmenorrhea

• One of the safest antipyretic drugs, especially for young infants (no risk of Reye's syndrome)

Novel Uses

1 g IV paracetamol was found to be equally effective as ketamine (0.5 mg kg21 bolus before induction, followed by 5 mg kg21 min21) when given prior to induction of anesthesia in preventing remifentanil-induced hyperalgesia, with the added benefit of a quicker time to extubating and full anesthetic recovery.

It has been demonstrated that combining paracetamol with the administered lidocaine during IV regional anesthesia enhances the overall effectiveness of the block. Lower intraoperative pain scores and total systemic analgesic doses resulted in earlier motor block onset, reduced tourniquet discomfort, and delayed recovery of motor and sensory block.

Side Effects:

- Liver Damage
- Skin reactions
- Asthma

Other usual side effects are as follows:

- Nausea
- Vomiting
- Stomach pain
- Loss of appetite
- Dark urine
- Yellowish skin

Dosage, Route, And Administration

Sr. No		DOSE	SINGLE DOSE	FREQUENCY	ROUTE	INSTRUCTIONS
1	Adults	500-1000mg	750mg	6 hours	Parenteral Oral	Maximum adult dose is 4g/day in divided doses (i.e., 1g every 6 hourly)
2	Paediatric	10-15mg/kg	12mg	6 hours	Oral	-
3	Neonatal	12mg/kg	12mg	6 hours	Oral	-

Clinical Pharmacology

Pharmacodynamics (Mechanism of Action)

It is interesting that the exact mechanism of action of paracetamol has not been identified after more than 100 years. Prostaglandin synthesis, serotonergic, opioid, nitric oxide (NO), and cannabinoid pathways are only a few of the fundamental processes that have been implicated in this process. It is also likely that several interconnected pathways are involved.

Prostaglandin inhibition (CO-X Inhibitor)

Paracetamol is termed a simple analgesic and an antipyretic. Despite enduring of COX relies on its being in the oxidized form and it is suggested that paracetamol interferes assertions that it acts by inhibition of cyclooxygenase (COX)- mediated production of prostaglandins, unlike non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol has been demonstrated not to reduce tissue inflammation. There are two proposed explanations for this.

- Prostaglandin H2 Synthetase (PGHS) is the enzyme that converts arachidonic acid into prostanoids (such as prostaglandins and thromboxanes), and it has two active sites. Cyclooxygenase is the name given to this enzyme. The two sites viz: Cyclooxygenase (COX) and the peroxidase (POX) sites. It takes two steps to convert arachidonic acid to prostanoids; the first step requires COX activity to create the unstable intermediate hydroperoxide prostaglandin G2 (PGG2), which is then transformed into prostaglandin H2 (PGH2) by POX. Indirectly contributing to this is the enzymatic activity, which serves as a reducing co-substrate at the POX site. Paracetamol is a powerful inhibitor of PG production in intact cells when arachidonic acid levels are low because it prevents the natural regeneration of POX. Prostaglandin synthesis is only marginally suppressed in damaged cells, where hydroperoxide levels are high. This peroxide-dependent COX inhibition explains why paracetamol acts differently at peripheral sites of inflammation from the brain, where peroxide concentrations are high with high peroxide levels

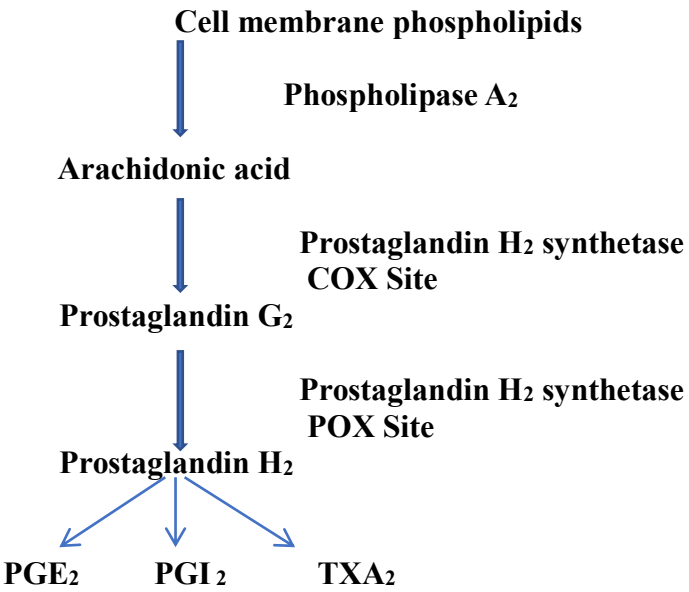


FIG. NO. 02: ROLE OF PARACETAMOL IN INHIBITION OF PROSTAGLANDINS PRODUCTION

- An additional hypothesis put forth was that paracetamol might affect a specific COX-1 splice variant, as opposed to NSAIDS which operate on COX-1 and -2. (Initially thought to be a distinct isoenzyme, COX-3). Since paracetamol's inhibition of this COX-1 version would explain why it lacks anti-inflammatory and anti-platelet effects in the central nervous system rather than at the location of damaged or inflamed tissue.

Endocannabinoid Enhancement:

Paracetamol is conjugated with arachidonic acid to form the active metabolite, N-arachidonoylphenolamine, in the presence of the enzyme fatty acid amide hydrolase (FAAH), which is primarily found in the central nervous system. (AM404). Analogous to the action of serotonin or norepinephrine reuptake inhibitors, AM404 inhibits the reuptake of the endocannabinoid, anandamide, from synaptic clefts, increasing cannabinoid receptor activation on the post-synaptic membrane. This would explain the feelings of calm, euphoria, and relaxation that many paracetamols' users report experiencing, which appear to be unrelated to analgesia.

Pharmacodynamics

Absorption:

Oral paracetamol is absorbed, mainly from the small bowel, by passive transport, and has high, though variable, bioavailability.

Distribution:

About 1/3rd of it is uniformly dispersed throughout the body after becoming protein-bound.

Metabolism & Excretion:

It is metabolized primarily in the liver by glucuronidation and sulphation to non-toxic conjugates, but a small amount is also oxidized via the cytochrome P450 enzyme system to produce the extremely toxic metabolite, N-acetyl-p-benzo-quinone imine. (NAPQI). Under typical circumstances, NAPQI is detoxified by combining with glutathione to generate conjugates of cysteine and mercapturic acid, which are then eliminated by means of the urinary tract.

Paracetamol Poisoning:

However, when glutathione levels are low or there is a glutathione deficiency, NAPQI interacts with cellular membrane molecules and results in acute hepatic necrosis (for example, in a paracetamol overdose).

Management

Gastric emptying or stimulation of regurgitation should be carried out if the patient is brought in early. To prevent further absorption, activated charcoal is administered directly or through a tube. As required, additional supportive measures should be done.

Specific Antidote

A 15-minute IV infusion of 150 mg/kg of N-acetylcysteine should be followed by a 20-hour IV administration of the same dosage. A different option is to administer 75 mg/kg orally every 4-6 hours for 2-3 days. It replenishes the glutathione stores of the liver and stops the binding of the toxic metabolite to other cellular components. If begun 16 hours or more after taking paracetamol, it is essentially ineffective.

Drug Interactions:

- Substances that promote gastric emptying increase paracetamol absorption (e.g., metoclopramide).
- Substances that reduce stomach emptying reduce paracetamol absorption (e.g., anticholinergic agents, and opioids).
- If administered within 1 hour of paracetamol, cholestyramine (ion exchange resin) reduces absorption.
- Combined use of enzyme-inducing drugs, such as carbamazepine, phenytoin, barbiturates, or isoniazid, should be avoided because it increases the risk of paracetamol toxicity.
- Probenecid reduces paracetamol clearance almost two-fold by blocking its conjugation with glucuronic acid.
- For combination treatment with probenecid, the paracetamol dosage should be reduced.
- Salicylamide (analgesic and antipyretic) may increase the half-life of paracetamol clearance.
- Paracetamol may also increase chloramphenicol concentrations.

Warnings & Precautions:

- If hypersensitivity responses occur, stop using paracetamol.
- Because paracetamol causes liver damage, you should consult your healthcare practitioner before taking this medication.
- Before taking paracetamol, obtain medical guidance if the patient has been diagnosed with kidney impairment.

GELATIN PROFILE

Gelatin is a product produced by partial hydrolysis of collagen which is generally derived from bones, skin, and white connective tissues of animals. In this process, the conversion of insoluble collagens into soluble gelatin is done, and as a result, a solid form of gelatin is obtained by purification and concentrating the solution which is formed during the hydrolysis process of collagen. Its solubility is found in a hot solution or mixture of glycerol and water and in 6N acetic acid, and partial insolubility in alcohol, fixed oils, chloroform, volatile oils, and ether.

Uses

Gelatin is incorporated in the preparation of pastes, pastilles, suppositories, coating tablets, and in the manufacturing of hard and soft capsule shells. It is also used for the microencapsulation of drugs and other industrial materials. Specially purified and pyrogen-free gelatins are available for intravenous injection and a grade with big 'Bloom strength' is used for making gelatin capsules and for bacteriological culture media. (17)

Structure:

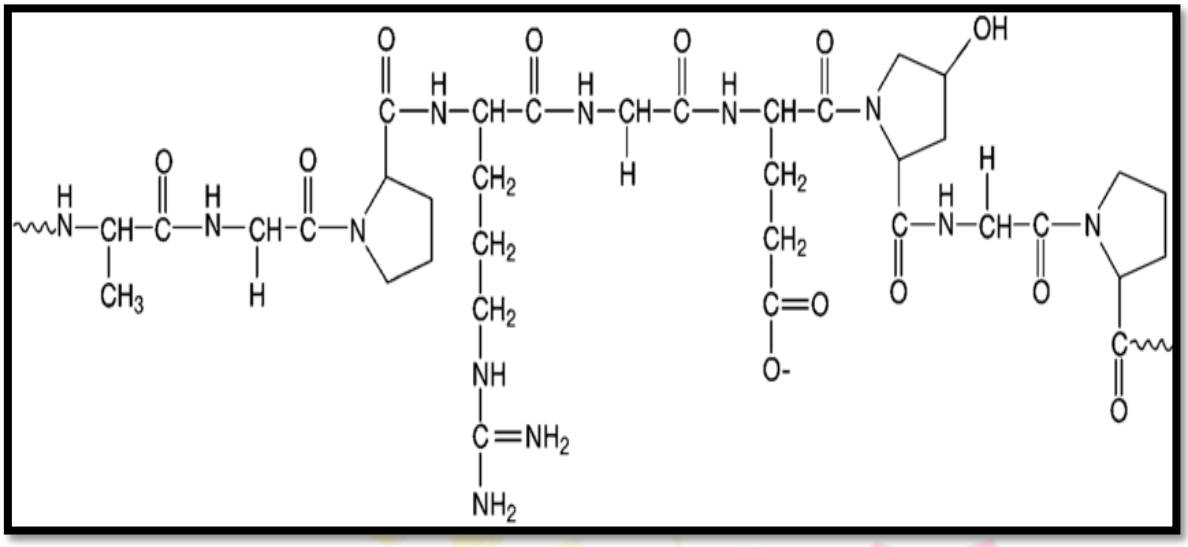


FIG. NO. 03: STRUCTURE OF GELATIN

Properties of complex gels of gelatin:

As per authors study the effects of aging time and composition on the thermomechanical properties of complex gels of gelatin and which had been produced based on complexes obtained at pH values below the isoelectric point of gelatin. With aging for up to 7 days, the elasticity of the gels decreases and the melting points are raised by 2-4 degrees C°. The development of an ion lattice and interaction between oppositely charged groups present in gelatin, result in an increment in heat which affects the stability of the gels. Also, hydrophobic interaction between nonpolar polar groups in this component is likely to be involved. (18)

Gelatin is a combination of polypeptide chains that forms a triple helical conformation. Every three chains in the triple helical conformation need around 21 residues to complete one spin. It comprises 50-1000 amino acids that are bonded cooperatively. Type I collagen is produced from the skin and bones and contains two α1 (I) chains and one α2 (I) chain. The two chains each have a molecular mass of k 95 kD with a width of ≈ 1.5 nm and a length of ≈ 0.3 μm. Inter-chain bonds are formed into the hydroxyl group bonds between the amino acid hydroxyproline with carbonyl peptides forming hydrogen bonds with water molecules. The stronger gel produces due to a higher amount of proline.(19)

Advantages:

- Gelatin is abundant in protein and has a distinctive amino acid profile that provides many positive health benefits and fulfils the daily protein requirement in the body.
- Gelatin may reduce joint and bone pain, elevate brain function, and helps to bring down the signs of skin aging. (20)
- It also contains antioxidants, which help to protect the cells in the body, that can assist the functions of the digestive system, bones, skin, joints, and other body functions.
- Consuming gelatin may help boost collagen levels and support skin elasticity.
- Consuming it as part of a balanced diet may help promote weight loss due to gelatin's high protein and low-calorie contents. (21)
- It promotes Good Sleep due to the presence of glycine in gelatin and can significantly improve the quality of sleep. (21)

- Gelatin can convert from a solid state to a melting state at body temperature. (22)

Disadvantages

- Daily consumption of about 15 grams of gelatin may result in side effects such as sour throat, swelling in gums, and mouth sores.
- It is non-vegan as it is derived from an animal. (23)
- Gelatin can cause allergic reactions such as anaphylactic shock to certain vaccinations that contain gelatin as a stabilizing agent. (24,25)

Applications:

- Gelatin is gluten-free.
- Gelling characteristic of gelatin is employed in the manufacturing of gummies.
- Gelatin is an aerating agent. It can be employed as an emulsifier, a stabilizer, a protective colloid, film-forming, water-binding, and an adhesive agent.
- Employed in the food industry, especially in desserts, candies, bakery products, jellied meat, ice cream, and dairy products. (26)
- Gelatin possess a hydrocolloid form and plays an vital role in enhancing the properties of industrial products.
- Gelatin has been employed as wetting agent, refined material, biodegradable packaging film, microencapsulation agent. (19)

Nutritional Values of Gelatin (24)

Nutritional values of gelation per 100g

NAME	VALUE PER 100 GRAM
Energy	429 kilocalories
Protein	100 grams
Total Fat	00
Carbohydrates	00
Total Sugar	00
Sodium	00

Nutritional Facts (27)

The many benefits of gelatin are due to its rich nutritional composition, which consists of:

COMPOSITION	NUTRITIONAL VALUE
Water	1 gram
Energy	381 kilocalories
Protein	7.8 grams
Carbohydrates	90.5 grams
Sugars	86 grams
Calcium	3 milligrams
Iron	0.13 milligrams
Phosphorous	141 milligrams
Magnesium	2 milligrams
Potassium	7 milligrams
Sodium	466 milligrams

The above values are for 100 grams of gelatin as per USDA database.

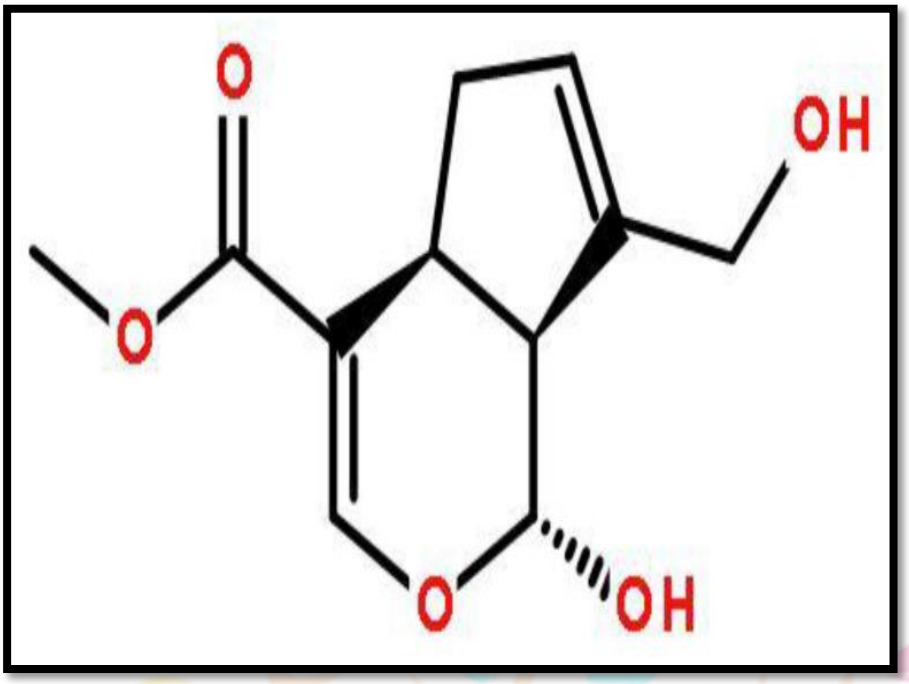


FIG. NO. 04: STRUCTURE OF HPMCK4M

Normal Quantity Used

5-10 %

Overdose

15 grams

HPMC K4M PROFILE

Introduction:

HPMC (hydroxypropyl methylcellulose) is a partly o-methylated and o-(2-hydroxyl propylated) cellulose, commonly it is also known as hypromellose. obtained by treating alkali, it can also be produced by synthetic modification of the naturally occurring polymer cellulose and is considered safe normal consumption in humans. it does not have any specific odor and taste and it is mostly available in granular and fibrous powder which are creamy white or white in color. Specifically, it is a modification of alkali cellulose, produced when purified wood pulp is treated with 18% sodium hydroxide solution. Methyl and hydroxypropyl ether groups and introduced into the molecule by reacting the alkali cellulose with methyl chloride and propylene oxide, respectively. HPMC is dissolved in cold water. We can prepare aqueous dispersion by dispersing at 80°C hot water while stirring vigorously. Enough cold water is added and mixed after complete hydration of HPMC. 50°C to 90°C is the range of gel point of HPMC. Gels are stable and have a wide range of pH (3-1). The interaction of HPMC polymer with colorants is rare. HPMC is an ideal polymer for film coating. When HPMC polymer is used alone, the polymer tends to bridge or fill the debossed tablet surfaces. A mixture of HPMC and other polymers or plasticizers is used to fill gaps problem.

HPMC produces a tough and flexible coating that is highly compatible, low cost, printable, non-allergenic, non-calorigenic, and more repellent to microbial attack. With the assistance of HPMC, not only controlled-release dosage forms often prepared but tablets with minimum efficacy and optimum speed can be manufactured. HPMC are cellulose ethers that are used as the basis for hydrophilic matrices for controlled release oral delivery. Despite the very fact that most of the pharmaceutical capsules which are available on the market are made up of gelatin, several HPMC capsules for powdered and dietary supplements are available in recent years.

Properties:

HPMC has various uses within the field of the controlled released dosage form. The functions are as follows:

- Thickening agent;
- As coating polymer in a controlled released dosage form;
- Bio adhesives;
- To enhance drug solubility in solid dispersion;
- As a binder in control released dosage form;
- Suspending agent;
- Water-holding property
- Stability

HPMC as a thickening agent

In interface agents, Hydroxypropyl MethylCellulose mainly functions because the thickening agent may increase the tensile strength and flexural strength. In interface agents, Hydroxypropyl MethylCellulose mainly operates because of the thickening agent and may increase the tensile strength and flexural strength. It also helps to enhance surface coatings, enhance adhesion, and improve the bonding strength of mortar Furthermore, good permeability can improve the uniformity of the interface, enhance lubricity and fluidity of mortar, make coating easier, and thus improve work efficiency The hydroxypropyl methylcelluloses have the identical character because of the pure methylcelluloses.

Hydroxypropyl methylcellulose (HPMC) is a water-soluble, high-purity, non-ionic cellulose ether. Methocel products function as thickeners, binders, and rheology modifiers. The mixture of properties presents simultaneously brings economic advantages versus other polymers.

Hydroxypropyl methylcellulose having a medium to high degree of substitution/ DS (1.5–2.0) is extremely soluble in cold water (0–30 °C (32–86 °F)). The solubility of HPMCs is improved compared thereupon to pure methylcelluloses. Transparent colloidal solutions of low to high viscosity are formed, counting on the degree of polymerization and therefore the substance concentration.

Like powdered methylcellulose, HPMC also tends to form lumps when transferred to cold water because of its high speed of hydration. Clear solubility and transparency are often increased by short-term cooling to 0–5 °C (32–41 °F).

Common uses of HPMC

Alternative to Gluten

HPMC also is an alternative to gluten in gluten-free food. If used while baking bread, it restricts the diffusion and loss of water from the bread crumb also as well as the interactions between starch and protein macromolecules. This gives a softer gluten-free bread and also reduces staleness during storage.

Alternative to Gelatin

HPMC is a suitable replacement for gelatin due to its physical similarity to gelatin and the vegetarian source. It is quite useful if you need to make your supplements since it can help vegetarians, also as well as those with dietary restrictions, consume supplements and medications.

Application

Coating:

The coating agent is formed into an organic solvent solution or aqueous solution for tablets, especially for the particles made from spray coating.

Slow Down Agent:

2-3 grams per day, each time 1–2-gram dosage, in 4-5 days to show the effect.

Eye Medicine:
The osmotic pressure of methylcellulose aqueous solution is the same as that of tears, it is small to the eyes, so it can act as an eye medicine, as a lubricant to contact the eyeball lens.

Gelatinous Agent:
Because of the base material of gelatinous external medicine or ointment.

Impregnating Drugs:
As a thickening agent, water retention agent.

Advantage

Surface Activity:
HPMC for a daily chemical aqueous solution has surface activity, ensuring its emulsification, protective colloid, and relative stability.

Low Ash Content:
The ions that exist in the product, within the preparation process we can use hot water washing for effective refinement, so its ash content is extremely low.

pH Stability:
HPMC aqueous solution viscosity in the range of pH 3.0-11.0 is more stable.

Disadvantage

Ingesting the compound can cause gastrointestinal distress also. While studies about this are contradictory, it is often hypothesized that HPMC is not well-received by the stomach.

Dosage Quantity:

The normal quantity used: 2%–5% w/w

EXPERIMENTAL PROCEDURES

NOTE: Temperature maintenance is key throughout the process.

PRELIMINARY STUDIES OF PARACETAMOL

DILUTIONS	Absorbance at 254nm
0.2	0.094
0.4	0.207

0.6	0.33
0.8	0.421
1	0.561
1.2	0.621
1.4	0.726

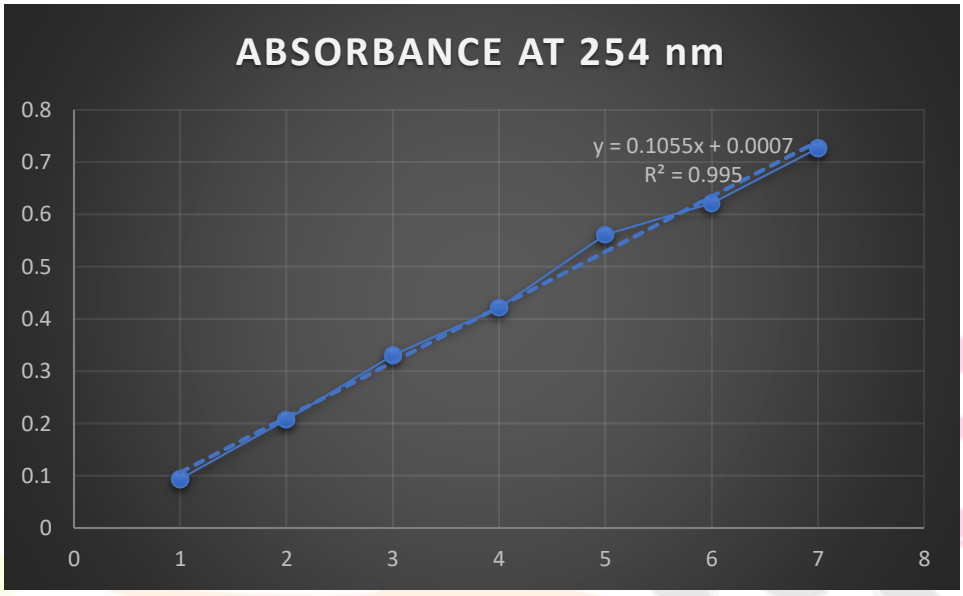


FIG. NO. 05: CALIBRATION CURVE OF PARACETMOL

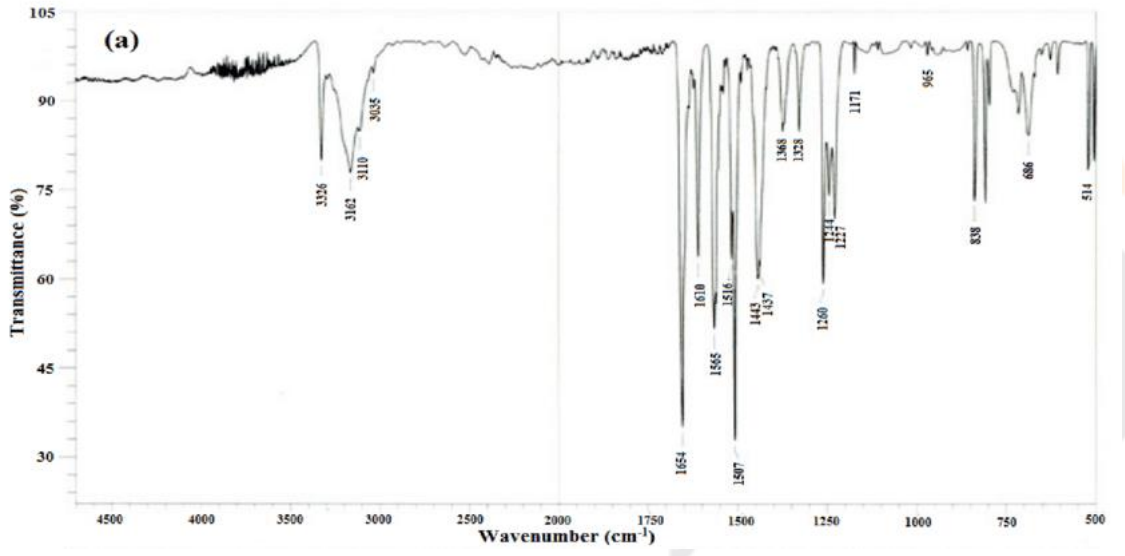


FIG. NO. 06: IR SPECTRA OF PARACEATMOL

EVALUATION SCREENING OF THE GUMMIES

1. **Appearance:**
   The appearance of gummies was observed for its smoothness, Clarity, Color, Homogeneity, Consistency and Presence of particles.

2. **Visual examination:**

Shape and Size was examined.

3. **Texture:**
The texture was tested by evaluating the hardness, softness.

4. **Determination of pH:**
The pH of solution was tested using digital pH meter.

5. **Viscosity:**
The Viscosity of the Solution was tested using Brookfield Viscometer, using Spindle number, at rpm

6. **Dissolution Study:**
Literature shows that the dissolution of gummies should be seen in 0.1 N HCl Solution. Invitro drug release study of gummies was carried out by using Paddle Apparatus method. The dissolution test was carried out using 900ml of 0.1 N HCl solution at 37 ± 0.50C and 100 RPM. A sample (5 mL) of the solution was withdrawn from the dissolution apparatus at 5, 10, 15, 20, 25, 30 min. and withdrawn volume was replaced with fresh dissolution media. Following parameters were used for the dissolution study.

1. **Apparatus:** USP dissolution apparatus type II (paddle type)
2. **Speed of the paddle:** 100 RPM
3. **Temperature:** 37.50c ± 0.50c
4. **Dissolution medium:** 0.1 N HCl
5. **Volume of fluid:** 900 mL
6. **Sampling time:** 5, 10, 15, 20, 25 and 30 minutes

7. **Stability Study:**
Stability was studied by preserving the gummies. The gummies were kept at different temperatures.

RESULT and DISCUSSION

1. Appearance:

TEST	OBSERVATION
Clarity	Clear
Color	Light Pink

2. Visual Examination:

Shape	Heart Shaped
Size	Length: 1.3 cm
	Height: 01 cm
	Width: 1.5 cm

3. Texture:

Hardness was tested by squeezing the gummy between the thumb and forefinger.

Softness was tested by bending the length.

4. Determination of pH:

The pH was tested using a digital pH meter. pH was found to be 7.2.

5. Viscosity:

Viscosity was measured using Brookfield Viscometer Model No. RVDVE Spindle number 02 for fixed time 2 minutes at the rotation of 3 revolutions per minute (25ºC ± 5º C).

6. Dissolution Study:

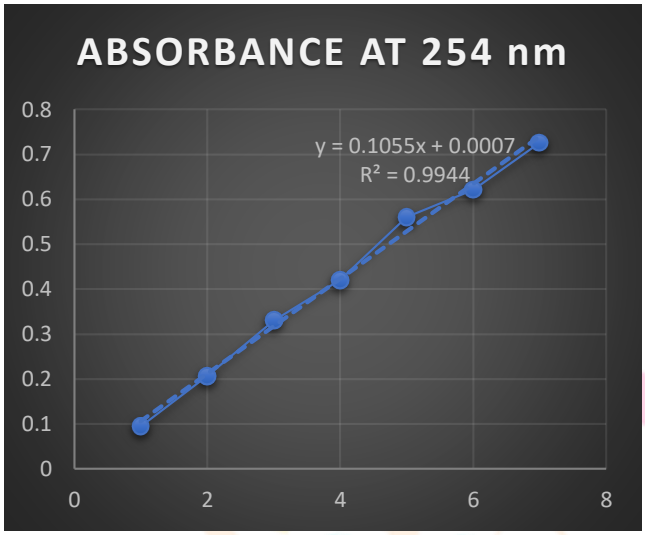


FIG. NO. 07: CALIBRATION CURVE OF PARACETAMOL

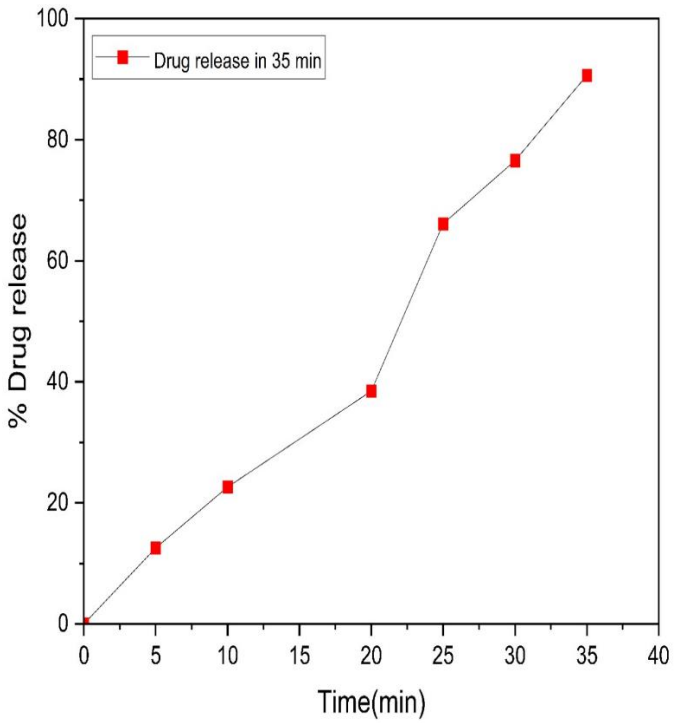


FIG. NO.08: DRUG RELEASE FROM THE GUMMIES (OPTIMISED FORMULATION)

CONCLUSION

It may be concluded that gummies can be prepared successfully using natural colorant strawberry crush and sweetener.

Experimentally is the optimized formulation which shows better viscosity during the formation of formulation it shows the better drug release. As it is in form of gummies it can be taken any time, any place.

REFERENCES

1. Graham GG, Davies MJ, Day RO, Mohamudally A, Scott KF. The modern pharmacology of paracetamol: therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings. Inflammopharmacology. 2013 Jun;21:201-32.
2. Chandrasekharan NV, Dai H, Roos KL, Evanson NK, Tomsik J, Elton TS, Simmons DL. COX-3, a cyclooxygenase-1 variant inhibited by acetaminophen and other analgesic/antipyretic drugs: cloning, structure, and expression. Proceedings of the National Academy of Sciences. 2002 Oct 15;99(21):13926-31.
3. Graham GG, Scott KF. Mechanism of action of paracetamol. American journal of therapeutics. 2005 Jan 1;12(1):46-55.
4. Raffa RB, Stone DJ, Tallarida RJ. Discovery of "self-synergistic" spinal/supraspinal antinociception produced by acetaminophen (paracetamol). Journal of Pharmacology and Experimental Therapeutics. 2000 Oct 1;295(1):291-4.
5. Ohashi N, Kohno T. Analgesic effect of acetaminophen: a review of known and novel mechanisms of action. Frontiers in Pharmacology. 2020 Nov 30;11:580289.
6. Goldstein JL, Brown MS. A century of cholesterol and coronaries: from plaques to genes to statins. Cell. 2015 Mar 26;161(1):161-72.
7. Ahmed AU. An overview of inflammation: mechanism and consequences. Frontiers in Biology. 2011 Aug;6(4):274.
8. Smith WL, Urade Y, Jakobsson PJ. Enzymes of the cyclooxygenase pathways of prostanoid biosynthesis. Chemical reviews. 2011 Oct 12;111(10):5821-65.
9. Aronoff DM, Neilson EG. Antipyretics: mechanisms of action and clinical use in fever suppression. The American journal of medicine. 2001 Sep 1;111(4):304-15.
10. Sullivan JE, Farrar HC. Fever and antipyretic use in children. Pediatrics. 2011 Mar 1;127(3).
11. Efe N. *Characterization and formulation of gelatin based soft candies* (Master's thesis, Middle East Technical University).
12. Schrieber R, Gareis H. Gelatine handbook: theory and industrial practice. John Wiley & Sons; 2007 Apr 20.
13. Ceschi A, Hofer KE, Rauber-Lüthy C, Kupferschmidt H. Paracetamol orodispersible tablets: a risk for severe poisoning in children?. European journal of clinical pharmacology. 2011 Jan;67:97-9.
14. Chabib L, Murrukmihadi M, Aprianto A. Pengaruh Pemberian Variasi Campuran Sorbitol Dan Glukosa Cair Sebagai Pemanis Pada Sediaan Gummy Candy Parasetamol. Jurnal Ilmiah Farmasi. 2013 Aug 5;10(2):69-77.
15. Gouveia TI. Development of vegan, sugar-free gummy candies-applicability to formulations with paracetamol.
16. Sabere AS, Suhaimi NA, Ahmed QU, Mahat MM, Roslan NC, Azizi J. Soft-chewable paracetamol tablets by melt granulation method: Formulation and characterization. Journal of Pharmacy & Bioallied Sciences. 2021 Jul;13(3):312.
17. Shanmugam S, Manavalan R, Venkappayya D, Sundaramoorthy K, Mounnissamy VM, Hemalatha S, Ayyappan T. Natural polymers and their applications.
18. Tschumak GJ, Wajnermann ES, Tolstogusow WB. Structure and properties of complex gels of gelatin and pectin. Die Nahrung. 1976 Jan 1;20(3):321-8.
19. Said MI. Role and function of gelatin in the development of the food and non-food industry: A review. InIOP Conference Series: Earth and Environmental Science 2020 Apr 1 (Vol. 492, No. 1, p. 012086). IOP Publishing.
20. Rowles A. What is gelatin good for? benefits, uses and more [Internet]. Healthline. Healthline Media; 2017 [cited 2023Apr11]. Available from: https://www.healthline.com/nutrition/gelatin-benefits

21. Gelatin: What it is made of, health benefits, nutrition, and more [Internet]. Medical News Today. MediLexicon International; [cited 2023Apr11]. Available from: https://www.medicalnewstoday.com/articles/319124#what-is-gelatin
22. Mark. Pros and cons of using gelatin [Internet]. UK Gummy Company. 2020 [cited 2023Apr11]. Available from: https://ukgummycompany.com/pros-and-cons-of-using-gelatin/
23. Gelatin: Overview, uses, side effects, precautions, interactions, dosing and reviews [Internet]. WebMD. WebMD; [cited 2023Apr11]. Available from: https://www.webmd.com/vitamins/ai/ingredientmono-1051/gelatin
24. Medically reviewed by Rowinda DimechRowinda Dimech, (Biotechnology) XVPMS, Patnaik VPV, Rdn, More, Writer H& W. Health benefits and side effects of gelatin [Internet]. STYLECRAZE. 2023 [cited 2023Apr11]. Available from: https://www.stylecraze.com/articles/gelatin/
25. Sakaguchi M, Inouye S. Systemic allergic reactions to gelatin included in vaccines as a stabilizer. Japanese Journal of Infectious Diseases. 2000 Oct 1;53(5):189-95.
26. Djagny KB, Wang Z, Xu S. Gelatin: a valuable protein for food and pharmaceutical industries. Critical reviews in food science and nutrition. 2001 Nov 1;41(6):481-92.
27. Gelatin: Powder, uses, types, benefits for health and side effects [Internet]. Google. Google; [cited 2023Apr11]. Available from: https://www.google.com/amp/s/www.myupchar.com/en/tips/gelatin-benefits-uses-side-effects.amp
28. Teixeira-Lemos E, Almeida AR, Vouga B, Morais C, Correia I, Pereira P, Guiné RP. Development and characterization of healthy gummy jellies containing natural fruits. Open Agriculture. 2021 Jan 1;6(1):466-78.
29. Moghaddas Kia E, Ghaderzadeh SL, Mojaddar Langroodi A, Ghasempour Z, Ehsani A. Red beet extract usage in gelatin/gellan based gummy candy formulation introducing Salix aegyptiaca distillate as a flavouring agent. Journal of Food Science and Technology. 2020 Sep;57:3355-62.
30. Renaldi G, Junsara K, Jannu T, Sirinupong N, Samakradhamrongthai RS. Physicochemical, textural, and sensory qualities of pectin/gelatin gummy jelly incorporated with Garcinia atroviridis and its consumer acceptability. International Journal of Gastronomy and Food Science. 2022 Jun 1;28:100505.
31. DeMars LL, Ziegler GR. Texture and structure of gelatin/pectin-based gummy confections. Food hydrocolloids. 2001 Jul 11;15(4-6):643-53.
32. Zhou XY, Yu JH, Yu H. Effect of gelatin content and oral processing ability on vitamin C release in gummy jelly. Journal of Food Science and Technology. 2021 Mar 10:1-9.
33. Rani KC, Jayani NI, Feneke F, Melanda S. Preparation and evaluation of gelatin and pectin-based Moringa oleifera chewable-gummy tablets. InIOP Conference Series: Earth and Environmental Science 2021 Nov 1 (Vol. 913, No. 1, p. 012082). IOP Publishing.
34. Meesang S, Wuttijumnong P, Pongsawatmanit R, Chenputhi S. Effect of gelatin sucrose/glucose syrup ratio and citric acid on physical properties and sensory quality of gummy jelly product. InProceedings of 41st Kasetsart University Annual Conference, 3-7 February, 2003. Subject: Agro-Industry 2003 (pp. 20-27). Kasetsart University.
35. Yan B, Davachi SM, Ravanfar R, Dadmohammadi Y, Deisenroth TW, Van Pho T, Odorisio PA, Darji RH, Abbaspourrad A. Improvement of vitamin C stability in vitamin gummies by encapsulation in casein gel. Food Hydrocolloids. 2021 Apr 1;113:106414.
36. Rutuja R. Khatode, Saniya B. Pathan, Pratik Datir, Shraddha Khaladkar. Formulation and evaluation of Multivitamin Gummies. International Journal of Advanced Research in Science, Communication and Technology. 2022;:391–9.
37. Lohar PB, Shrivastav P, Kulavoor S. [PDF] development of fiber rich gummies: Semantic scholar [Internet]. International Journal of Advance Research, Ideas and Innovations in Technology. 1970 [cited 2023Apr11]. Available from: https://www.semanticscholar.org/paper/Development-of-fiber-rich-gummies-Lohar-Shrivastav/49758a9283a743ae04fc144ead775032b1c553b1