JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

ENHANCEMENT OF NUTRITIONAL VALUE OF GUMMY CONFECTIONARY FOOD BY INCORPORATING EPIGALLOCATECHIN GALLATE AND SERVING AS A DISEASE-PREVENTIVE TOOL.

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Abstract : Nutraceutical-based gelatin gummy bears incorporated with epigallocatechin gallate being an antioxidant provide various health benefits as it prevents ailments like cancer and diabetes. This study involves the development of 8 different formulations each prepared with 5%, 7.5%, 10%, and 20% of gelatin and each formulation was combined with 26% and 16% concentration of honey. Formulation with 10% gelatin and 16% honey was optimized after carrying out appearance, elasticity, transparency, swelling ratio, and dispersion time test. *In vitro* release profile of the optimized formulation was found to release 50 % of the drug within 14 minutes of the dissolution process and was completely released within 25 minutes. The DPPH free radical activity showed 0.107 absorbance at 517 nm with 49.04 % of scavenging activity. The texture of the formulation was found optimum after carrying out its texture analysis using TA.HD. Plus texture analyser.

1. Introduction

The use of nutraceuticals for services like illness prevention and promotion is expanding rapidly. In addition to being used for nutrition, nutraceuticals have also been employed as a support therapy for the prevention and treatment of several diseases, such as to lessen the negative effects of radiotherapy and chemotherapy for cancer.[1]

Due to the many benefits it offers, the oral administration route is favored above the various other administration methods of medication delivery. These benefits include security, excellent patient compliance, the convenience of consumption, pain prevention, and adaptability to accept a variety of medications.[2] Due to the highest component of compliance, it is well recognized that the oral route is the most practical method for the administration of active Substances in food supplements, functional food items, etc.[3]

Confectionaries have a wide range of uses in the food and pharmaceutical industries as new medication delivery systems that are more appealing to kids and certain adults due to their appearance and flavor.[4] According to reports, the jellifying agent (pectins, modified starch, gelatin, etc.) and sugars make up the majority of a gummy bear's basis, allowing water-soluble elements to dissolve and insoluble ones to be suspended in the viscous matrix.[5]

According to the study conducted by Rodriguez-Pombo et. al. (2022) Gummies are utilized for systemic drug distribution because the buccal mucosa is the site of drug absorption. Drugs that are immediately absorbed through the mucous membranes of the oral cavity avoid the first-pass effect and GI tract degradation. However, medications that are released but not absorbed in the mouth dissolve or scatter in saliva and are ingested through the stomach. As a result, adding buccal absorption to gummy formulas could increase their bioavailability and hasten the therapeutic effect.[6]

However, the use of gummy bears as food supplements or nutraceuticals is restricted because they often contain over 50% sugar, which has little nutritional benefit and raises the risk of developing health issues like coronary and heart disease.[7],[8]. According to the study conducted by Andreu Fernande et. al. (2020), due to the first-pass effect, epigallocatechin gallate has a bitter taste and low absorption. Additionally, EGCG taken with dietary supplements increased the molecule's stability in the body.[9]

Flavonoids are among the most prevalent kinds of plant phenolics. Given their role in food organoleptic qualities and human health, a better knowledge of their structures and biological activities points to their potential as therapeutic agents as well as for predicting and monitoring food quality. Due to their extensive range of pharmacological activity in the mammalian body, flavonoids are more aptly referred to be "nutraceuticals" instead.[10]

Due to the high percentage of people in need and its benefits in combating conditions like cancer, heart disease, diabetes, and obesity, among others, epigallocatechin gallate was chosen as the active ingredient to add to the base of the gummy bears.[11] Masking the bitter taste of epigallocatechin gallate is a challenge. Together, green tea and honey balance each other's effects and counteract the harshness of the tea. Since the dawn of time, honey and green tea have been used in China as a common beverage and pharyngitis cure.[12]

Therefore, the goal of our study was to create gummy bears based on nutraceuticals and evaluate the appropriate concentration of gelatin for use in pharmaceuticals, dietary supplements, or confectionary manufacturing.

Gelatin is a viscoelastic material with the characteristics of gumminess. The origin of the source collagen and the rigor of the extraction processes impact the qualities of the finished gelatin14. Gelatins are generated from the parent protein collagen. In the production of food goods, gelatin products with a variety of Bloom and viscosity values are used, with particular attributes are chosen based on the requirements of the application. Collagen peptides may have 'nutraceutical' qualities, meaning that consuming them has positive physiological effects. An extremely robust collection of clinical evidence demonstrates how taking a specific collagen peptide helps osteoarthritis patients experience less pain and better joint function.[13].

2. Materials and methods

2.1 Material

Epigallocatechin gallate was purchased from Yucca Enterprises, dabur honey was purchased from the pharmacy, citric acid and propylene glycol were purchased from Vishal Chem (Mumbai) and Gelatin powder Extra Pure (Bacto) was purchased from S D Fine-Chem Limited (Mumbai), sodium benzoate was purchased from Research Lab Fine Chem Industries (Mumbai).

2.2 Method

2.2.1 Preparation of gelatin-based epigallocatechin gallate gummies.

Gelatin-based gummies were prepared by heating and congealing method. Epigallocatechin gallate was incorporated into the Gelatin base and natural sweetener like honey was used along with citric acid as a pH corrector, sodium benzoate as preservative and propylene glycol as an appearance enhancer. Gelatin was allowed to bloom in water for 10 minutes in a little amount of water. Water, honey, citric acid, and propylene glycol were mixed and subjected to heat and then sodium benzoate and epigallocatechin gallate respectively, were added to it with continuous stirring. Bloomed gelatin was added part by part to the above mixture on flame with continuous stirring to form a homogenous mixture. The temperature was maintained between 115-120^{0}C . The mixture was filled into molds and refrigerated for 2 to 3 hours.

2.2.2 Evaluation of prepared gelatin gummy formulation.

2.2.2.1 Organoleptic observations

The prepared gummy's color, shape, and texture were assessed organoleptically. By lightly stroking the surface of the tablets between two fingers, the texture was observed.[14]

2.2.2.2 weight variation test

To assess the homogeneity of each gummy's content, weight variation was measured. At first, at least 20 individual gummies were weighed, and the average weight was then determined.[14]

2.2.2.3 Swelling ratio test

A quick way to assess a gel structure's ability to absorb water is to do a swelling ratio test. After being weighed, 3 gummies from each batch were submerged in 100 ml of sterile water for 30 minutes. The remaining water on the tablet's surface was wiped off with filter paper before the second weight. By dividing the weight difference between the tablet's initial weight and its weight after immersion, the swelling ratio was computed.[14]

2.2.2.4 Dispersion time test

Three Gummies from each formulation were subjected to the dispersion test in a flask with 100 ml of pure water at 37°C. Each formulation's gummy was added to the flask and vigorously swirled using a magnetic stirrer. It was timed to see how long it took for it to disperse. The recommended dispersion time for gummies is 10–30 minutes.[14]

2.2.2.5 *In vitro* release profile

900 ml of artificial saliva at 37 0.5°C served as the dissolution media in the Dissolution Test Apparatus II. 150 rpm was used to operate the paddles. The 60-minute dissolution period was chosen. Calculations were made to determine the amount of dissolved epigallocatechin gallate in the medium.[15]

2.2.2.6 Texture analysis

TA.HD Plus texture analyzer was used to accomplish the texture analysis. The gummy was first placed in the sample testing area, after which the probe was fitted inside the area, and several parameters, including firmness, springiness, hardness, stickiness, strength, and flex, were set to conduct the test.[3]

1. Compression test
   The probe then continues to compress the sample to 20% of its original height after reaching the trigger force of 5g. After maintaining this distance from the sample for 60 seconds, it returns to its initial position.

2. For the penetration test, With a trigger force of 20 g and a load of 5 kg, an analytical probe p/6 was pushed down into each gummy bear sample and penetrated it at a predetermined rate (1 mm/s) to a certain depth (5.0 mm). The graph's maximum force value represents the hardness of a gummy. A higher peak load indicates a harder gummy bear with lower penetration.
3. Flexibility test
   If and when the distance between the blade and the two adjustable supports was equal, the heavy-duty platform was set up correctly. The sample was positioned in the center of the supports further on. Each gummy bear had the probe pushed down into it at a rate of 2 mm/s with an automated trigger force utilizing a load of 5 kg.[3]

2.2.2.7 DPPH assay

DPPH is a stable artificial free radical that has been frequently used to evaluate the ability of phenolic compounds to scavenge free radicals in ethanol and aqueous solutions. In a nutshell, 2 mL of sample solution at various concentrations were incubated with 2 mL of 0.2 mM DPPH solution in 95% ethanol. The reaction mixture was then mixed and kept at room temperature for 40 minutes. Using a spectrophotometer, the absorbance was instantly measured at 517 nm against ethanol. The following formula was used to compute the DPPH free radical scavenging rate: DPPH scavenging activity(%)=A0−A1A0×100.[16]

3. Result and discussion

A study prepared gelatin gummies containing epigallocatechin gallate using gelatin as a gelling agent, honey was used as a natural sweetener, citric acid used as pH corrector sodium benzoate and propylene performs the role of preservative. Propylene glycol also enhanced the glossy appearance of the gummy bear, brown food color was added to enhance the appearance and make it more appealing.

Table 1. Formulation table of gelatin-based epigallocatechin gallate gummies

Sr. no.	Ingredients	F1 %	F2 %	F3 %	F4 %	F5 %	F6 %	F7 %	F8 %
1	EGCG	10	10	10	10	10	**10**	10	10
2	Gelatin	5	5	7.5	7.5	10	**10**	20	20
3	Honey	26	16	26	16	26	**16**	26	16
4	Citric acid	1	1	1	1	1	**1**	1	1
5	Sodium benzoate	0.5	0.5	0.5	0.5	0.5	**0.5**	0.5	0.5
6	Propylene glycol	4	4	4	4	4	**4**	4	4
7	Brown food color	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	**Q.S.**	Q.S.	Q.S.
8	water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	**Q.S.**	Q.S.	Q.S.

Gelatin served as an emulsifier, a binder that reduced brittleness and facilitate molding. The hardness of the gummy confectionary increased with an increase in the concentration of gelatin. Honey was served in retaining moisture that kept gummies moist when added 16% and was a healthier alternative to all synthetic sweeteners. After 25 to 30 days gummies were prone to microbial contamination which was prevented by adding preservatives.

The formulation of gelatin gummies was prepared with trials of different concentrations of gelatin and honey. The concentrations tried were 5%, 7.5%, 10%, and 20% of gelatin and 26% and 16% of honey, out of which the gummies from batch F1 were found to be too sticky and watery, it was observed that the stickiness and moisture entrapment was due to high honey and low concentration of gelatin, so we increased the concentration of gelatin ascendingly and decreased the concentration of honey to obtain desired gummy bears. A batch with 10% gelatin and 16% honey was found to be optimum with the desirable hardness and elasticity of the formulation.

Figure 1. Image of F6- optimized Gelatin Gummy formulation which has 10% and 16% concentration of gelatin and honey respectively.

Table 2. Physical characteristics of the prepared epigallocatechin gallate chewable-gummies

Evaluation parameters	F2	F4	F6
Organoleptic properties			
Color	Brown	Brown	Brown
Shape	Bear shaped	Bear shaped	Bear shaped
Texture	Sticky Less elastic	Moderately sticky Moderately elastic	Non-sticky Elastic
Weight variation test	2.39g	2.48g	2.46g
Swelling ratio test	1.35	2.3	2.65
Dispersion time test	12.5 min	16.4 min	23.3 min

As per observation, gummies were found to be brown in color, bear-shaped, elastic, and glossy. 20 gummies in this study weighed between 2.34-2.56 grams, The results showed that no individual gummy exceeded the weight in the pharmacopeial requirement, implying that all the prepared gummies contained a homogenous amount of epigallocatechin gallate. The swelling ratio test was intended to evaluate the ability of the gummy to absorb water molecules inside its structure. The higher the swelling ratio, the higher the gummy's ability to entrap water molecules and it was found to be 1.35, 2.3, 2.65 for F2, F4, and F6 formulations respectively out of which F6 formulation shows good swelling. A dispersion time test was conducted to estimate how quickly the gummies dissolved in aqueous media to ensure dissolution upon contact with saliva. Faster dispersion time indicates faster release of the active ingredients from a dosage form. The gummy formulation was found to disperse within 12.5, 16.4, and 23.3 minutes for F2, F4, and F6 formulations respectively.

As the F6 formulation was found to be non-sticky, elastic, good swelling ratio, and dispersion within limits it was further subjected to *In vitro* dissolution studies, texture analysis, and *In vitro* antioxidant activity. *In vitro* dissolution study was performed based on the possibility that a patient might swallow the dosage form without proper chewing. 50 % drug was released within 14 minutes of the dissolution process and was completely released within 25 minutes. By using 1,1-diphenyl-2-picrylhydrazyl (DPPH) the radical scavenging activity was determined. When an active compound reacts with DPPH it transfers an electron or hydrogen atom and neutralizes its free radical character. Ascorbic acid was taken as a reference standard for free radical scavenger activity and test sample compared. Prepared dilute solution observed under UV spectrophotometer and absorbance detected at 517 nm. When absorbance decreases the percentage of radical scavenging activity increases. It can be observed from Table 2 that the antioxidant activity of epigallocatechin gallate showed 0.107 absorbance at 517 nm with 49.04 % of scavenging activity. Texture analysis was carried out for F6 formulation and
it was found to be within limits according to the literature review on reported studies.

Figure 2 illustrates a force-time (or distance) curve which shows the characteristics of a gum firmness and springiness test.

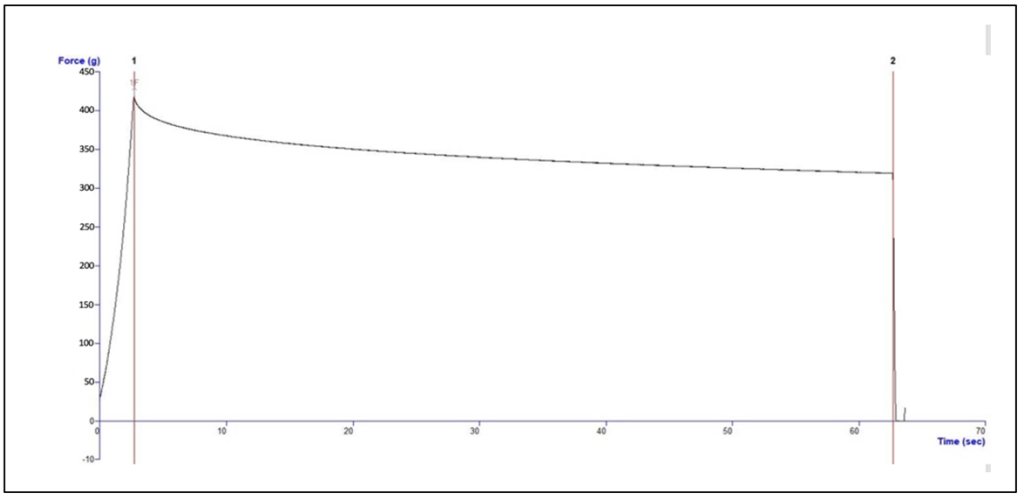

Figure 2. Graph of compression test showing firmness and springiness of the formulation. 1 represents deforming force required to bend the sample, higher the force required to bend, firmer the sample. 2 represents the rate at which a deformed material goes back to its undeformed condition after deforming force is removed.

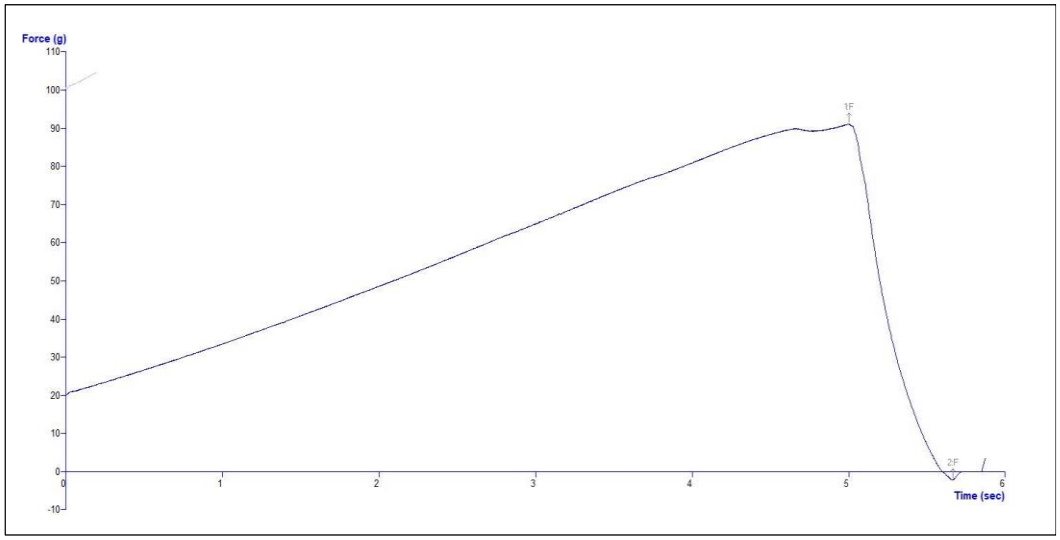

Figure 3. Graph of penetration test showing hardness(1F) and stickiness (2F). The graph's maximum force value represents the hardness of a gummy. Stickiness is the force necessary to overcome the attractive forces between the surface of a product and surface of probe.

Figure 4. Graph of Flexibility test showing strength and distance at flex. The product began to bend once the trigger force was reached, as the value of force increased. The greatest point of force was defined as the gummy bear's resistance to bending. The sample's strength is related to the force's value. The distance at which the force peaks is measured, highlighting the amount of deformation that must be given to the material before full bending begins, and defining flexibility.

Table 2. The results of firmness, springiness, hardness, stickiness, strength, and distance at flex.

Sr. No.	1		2		3	
Test	Compression test		Penetration test		Flexibility test	
	Firmness	Springiness	Hardness	Stickiness	Strength	Distance at flex
Result	400.62 g	66.63 %	91.22 g	-2.28 g	217.44 g	14.58 mm

4. Conclusion

A gummy formulation with 10% gelatin and 16% honey was optimized owing to its appearance, elasticity, transparency, swelling ratio, and dispersion and was evaluated further for its texture, antioxidant activity, and *in vitro* drug release profile in case the patient gulp it by mistake. Confectionaries usually contain high sugar values which decreases their nutritional value but here in this case we have prepared the gummy bears with high nutritional value by substituting sugar with honey. The combination of honey and gelatin neutralized the bitter taste of EGCG. EGCG has low gastric and intestinal solubility, which reduces its bioavailability, in the case of gummies drug absorption occurs through the buccal mucosa via the membranes lining the oral cavity bypassing the first-pass effect and avoiding degradation in the GI tract.

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