

Original Article

## FORMULATION AND EVALUATION OF COSTUS IGNEUS HERBAL LOLLIPOPS FOR DIABETES MANAGEMENT

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Received: 07.11.2024 / Accepted: 23.01.2025 / Published: 22.04.2025

### ABSTRACT

**Objectives:** This study aims to develop and evaluate the efficacy of herbal lollipops incorporating *Costus igneus* extract for diabetes management. **Materials and Methods:** The powdered *Costus igneus* material was subjected to extraction using ethanol by Soxhlet extraction method. The extract was filtered and concentrated under reduced pressure to obtain a concentrated extract. Various formulations of herbal lollipops were prepared using different concentrations of *Costus igneus* extract, along with suitable excipients like stevia, binder and colors. **Results:** The formulated lollipops showed the uniformity in weight and thickness. The hardness of all formulated lollipops was found within the standard range up to 9.65 to 10.50 kg/cm<sup>2</sup>. From the *in-vitro* drug release study, it was found that the formulations of lollipops containing corn syrup in the concentrations of 100, 90 and 80 mg showed the maximum drug release at 30 minutes. Among those formulations formulation F9 showed 100.6% of drug release. The *in-vitro* release kinetic study of the optimized formulation (F9) was found to be first order. The release of the dosage form follows the diffusion and dissolution mechanism and Non-Fickian diffusion mechanism. **Conclusion:** These findings suggest that herbal lollipops containing *Costus igneus* hold promise as a novel and effective alternative for managing diabetes.

**KEYWORDS:** *Costus igneus*, Diabetes, Soxhlet extraction, herbal lollipops.

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### 1. Introduction

*Costus igneus*, commonly known as the insulin plant, has long been recognized in traditional medicine for its potential anti-diabetic properties. The plant, native to parts of Asia and Central America, has gained popularity for its purported ability to help regulate blood glucose levels in individuals with diabetes mellitus [1-4]. Research into its bioactive components has highlighted compounds that may mimic insulin-like actions, thereby contributing to the management of hyperglycemia. As such, *Costus igneus* has become a subject of considerable interest in modern phytotherapy for its potential role in diabetes management [5].

Traditional uses of *Costus igneus* predominantly involve consuming the leaves or extracts, which are believed to have therapeutic effects on blood sugar regulation. These practices, rooted in centuries of use, have spurred modern investigations into the pharmacological mechanisms of the plant. Current studies have indicated that *Costus igneus* may enhance insulin sensitivity and improve pancreatic function, which could be beneficial for individuals with type 2 diabetes [6-9]. However, while these findings are promising, the bioavailability of its active compounds remains a challenge, particularly when consumed through conventional forms such as raw leaves or infusions.

In recent years, there has been a growing interest in innovative pharmaceutical delivery systems to enhance the therapeutic efficacy and patient compliance of herbal remedies. One such novel formulation is the herbal lollipop, which offers a palatable, convenient and non-invasive alternative to traditional herbal administration. Herbal lollipops are especially appealing to diabetic patients who may face difficulties with swallowing pills or consuming bitter herbal extracts. By encapsulating the beneficial compounds of *Costus igneus* in a lollipop format, these formulations could provide a more accessible and enjoyable method of delivering the plant's therapeutic properties [10].

The primary research problem addressed in this study is the formulation and evaluation of *Costus igneus*-based herbal lollipops as an effective, palatable and convenient dosage form for diabetes management. The novel approach of herbal lollipops could improve patient compliance and make it easier to incorporate the therapeutic properties of *Costus igneus* into daily diabetic care. Additionally, this research is vital to ensure the stability, efficacy, and safety of herbal lollipop formulations.

## 2. Materials and methods

### 2.1. Collection and preparation of *Costus igneus* extract

Fresh leaves of *Costus igneus* were collected from a local herb garden. The leaves were carefully washed with distilled water to remove dirt and impurities, then dried under shade conditions to prevent degradation of bioactive compounds. Once dried, the leaves were ground into a fine powder. The extraction of active compounds was performed using the Soxhlet extraction method with ethanol as the solvent. The powdered material was placed in the Soxhlet apparatus, and ethanol was allowed to extract the bioactive components over several cycles. After extraction, the resulting liquid extract was filtered to remove any residual plant material, and the filtrate was concentrated under reduced pressure using a rotary evaporator to obtain a concentrated *Costus igneus* extract [11-14].

### 2.2. Determination of melting point of quercetin

Determination of the melting point of the drug was done using an electrical melting point apparatus, capillary method [15].

### 2.3. Determination of $\lambda_{\max}$ of quercetin

A 2000 ppm methanol solution of quercetin was prepared and scanned using a spectrophotometer in the range of 400-800 nm to establish the drug's  $\lambda_{\max}$ , while Fig. 1 illustrates the spectrum of the quercetin [16].

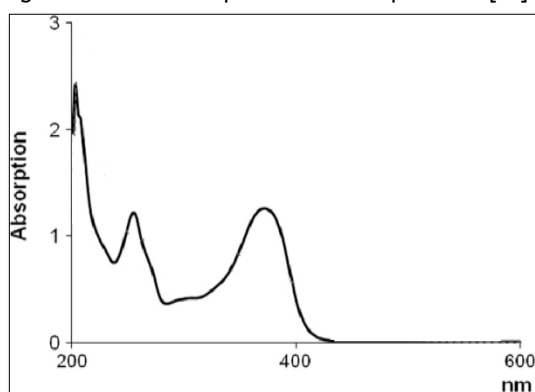


Fig. 1. UV spectrum of quercetin in ethanol

### 2.4. Drug-excipient compatibility studies

The preparation of a dosage form involves taking into account elements that relate to the physicochemical properties of the drug substances and the other components used, known as excipients. When it comes to the creation of an effective and stable dosage form, the choice of right excipients is of paramount importance. In this case, the drug and excipients have to be compatible in order to yield a stable, effective, easy to handle and safe product. As a result compatibility was tested by Fourier Transform Infrared Spectrophotometry (FTIR) by using potassium bromide pellet method. The spectra obtained were studied and analyzed for the study. The Table 1 presents the pertinent data of FTIR spectral interpretation of quercetin, while Fig. 2-4 illustrate the FTIR spectra of compatibility studies [17-19].

Table 1. FTIR Spectral Interpretation of Quercetin

| S. No. | Peak Value          | Functional Groups |
|--------|---------------------|-------------------|
| 1      | 3406 and 3283       | OH                |
| 2      | 1379                | Phenol            |
| 3      | 1666                | Aryl ketonic      |
| 4      | 1610, 1560 and 1510 | Aromatic ring     |
| 5      | 1317                | In plane aromatic |
| 6      | 1263                | Aryl ether        |
| 7      | 1200                | Phenol (C-O)      |
| 8      | 1165                | Ketone (C-CO-C)   |

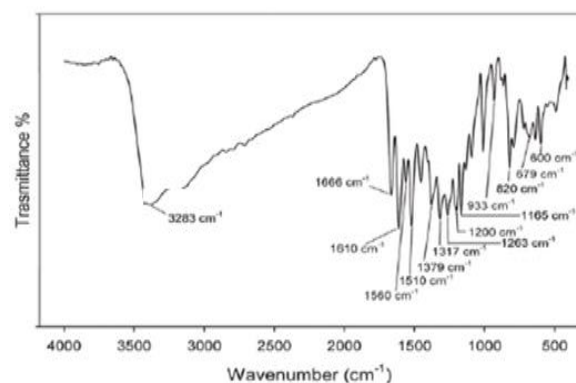


Fig. 2. FTIR spectrum of drug + Stevia sugar

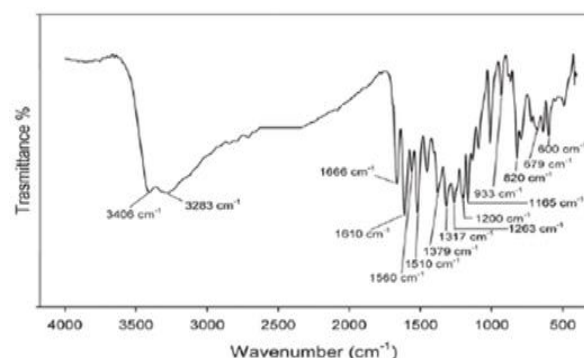


Fig. 3. FTIR spectrum of drug + corn syrup

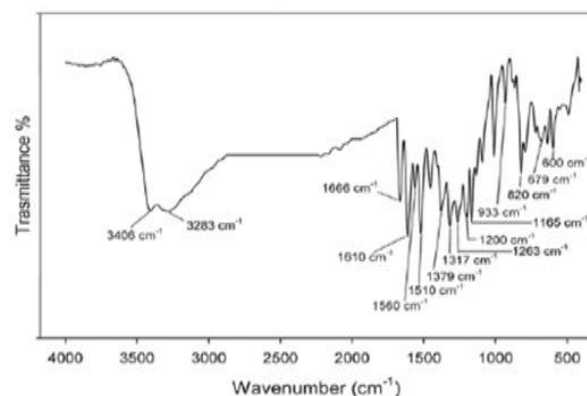


Fig. 4. FTIR spectrum of drug + glycerine

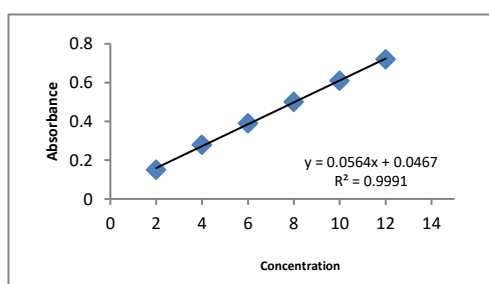
### 2.5. Preparation of calibration curve for quercetin

Creating a calibration curve for quercetin involved weighing 100 milligrams of the substance and transferring it into a 100 milliliter volumetric flask. The quercetin was dissolved in methanol, and the volume was adjusted to 100 milliliters to create a stock solution with a concentration

of 1000 micrograms per milliliter ( $\mu\text{g/ml}$ ). Portions of 0.2, 0.4, 0.6, 0.8, 1.0, and 1.21 milliliters of this stock solution were further diluted with methanol to 100 milliliters, resulting in solutions with concentrations of 2, 4, 6, 8, 10, and 12  $\mu\text{g/ml}$ . Subsequently, the solutions were scanned at 375 nanometers using a double-beam UV-Visible spectrophotometer. The Table 2 presents the pertinent data, while Fig. 5 illustrates it.

**Table 2.** Concentration and Absorbance of Quercetin

| Concentration ( $\mu\text{g/ml}$ ) | Absorbance |
|------------------------------------|------------|
| 2                                  | 0.15       |
| 4                                  | 0.28       |
| 6                                  | 0.39       |
| 8                                  | 0.5        |
| 10                                 | 0.61       |
| 12                                 | 0.72       |



**Fig.5.** Calibration curve for quercetin

## 2.6. Quantitative chemical tests of *Costus igneus* extract [20-22]

### 2.6.1. Test for tannins

For testing tannins, 0.5 g of powdered sample prepared from *Costus igneus* was boiled in 20 ml water and filtered through Whatman No. 6 paper filter. Filtrate was treated with few drops of 0.1% ferric chloride solution. A brownish-green or blue-black color is indicative of the presence of tannins. The extract tested positive in this test.

### 2.6.2. Test for flavonoids

The presence of flavonoids was tested using 1 ml methanolic extract, mixed with alcohol – 0.5 ml; magnesium – a pinch and concentrated HCl – a few drops. The presence of flavonoids will be supported by red color formation. The result was positive as shown by the extraction, indicating that it contains flavonoids.

### 2.6.3. Terpenoids test (Salkowski test)

The extract (5.0 ml) was shaken with chloroform (2.0 ml), for the detection of terpenoid: concentrated sulfuric acid [ $\text{H}_2\text{SO}_4$ ] 2.0 ml was added along sides of test tube. Reddish-brown color at the interface indicates terpenoids. Positive result: all coloration appears only in the extract.

### 2.6.4. Test for alkaloids

0.1 mg of the extract was dissolved in 10 ml of dilute hydrochloric acid (HCl) and filtered to test for the presence of alkaloids. Dragendorff's reagent (a), Mayer's formalin-boric acid reagent (b), and Wagner's iodine-KI reagent were then added. These reagents react with alkaloids, confirming their presence. A positive test result indicated the presence of alkaloids in the extract.

### 2.6.5. Mayer's test for alkaloids

1 ml of Mayer's reagent (potassium mercuric iodide solution) was added to a portion of the filtrate from the alkaloid test. The formation of a cream-colored precipitate indicated the presence of alkaloids, confirming a positive result for the extract.

### 2.6.6. Test for saponins (froth test)

The extract was shaken with 10.0 ml of distilled water in a test tube to test for saponins. If frothing persists even after warming for 5 minutes, saponins are present. This test was negative, as the extract did not foam significantly.

### 2.6.7. Test for anthocyanosides

1 mg of the extract was taken and poured in 5 ml diluted HCl. The development of pale pink color in the solution confirmed presence of anthocyanosides. The extract was found to test positive for these compounds.

### 2.6.8. Test for reducing sugars

Reducing sugars in the preparation were estimated by adding a 1.0 ml aliquot to dilute HCl, then making the solution alkaline with NaOH. The mixture was then subjected to a reaction with Fehling's A and B solutions under heating. The formation of a red precipitate indicates the presence of reducing sugars. No red precipitate indicates a negative result (Example: Extract).

### 2.6.9. Test for steroids

Steroids were detected by adding 2 ml of acetic anhydride and then 2 ml sulfuric acid to the methanolic extract (0.5 g). Color shift – Violet > Blue / Green → the presence of steroids. The extract demonstrated this color change which confirmed the presence of steroids.

## 2.7. Methodology

The herbal lollipops using *Costus igneus* were prepared using the formulas presented in Table 3 and Fig. 6 presents the optimized formulation [23].



**Fig. 6.** Optimized formulation of medicated lollipops

## 2.8. In vitro antidiabetic property of the extract

To evaluate the antidiabetic potential of *Costus igneus* extract, an in vitro glucose uptake assay was performed using L6 myotubes. The cells were exposed to varying concentrations of the extract, followed by glucose addition, and the glucose uptake was measured spectrophotometrically. The results demonstrated that the *Costus igneus* extract enhanced glucose uptake in a dose-dependent manner, indicating its potential antidiabetic activity. This finding suggests that *Costus igneus* may help regulate blood glucose levels by promoting glucose utilization in cells, likely due to its bioactive compounds such as flavonoids, tannins, and terpenoids.

**Table 3.** Formulation Table for Quercetin Medicated Lollipops

| Ingredient           | Composition per Lollipops |      |       |      |      |       |      |      |      |
|----------------------|---------------------------|------|-------|------|------|-------|------|------|------|
|                      | F1                        | F2   | F3    | F4   | F5   | F6    | F7   | F8   | F9   |
| Quercetin (mg)       | 500                       | 500  | 500   | 500  | 500  | 500   | 500  | 500  | 500  |
| Active Ingredient    |                           |      |       |      |      |       |      |      |      |
| Distilled Water (ml) | 60                        | 60   | 60    | 60   | 60   | 60    | 60   | 60   | 60   |
| Stevia sugar (mg)    | 200                       | 200  | 200   | 200  | 200  | 200   | 200  | 200  | 200  |
| Acacia Gum (mg)      | 0.070                     | 0.05 | 0.025 | -    | -    | -     | -    | -    | -    |
| Xanthan Gum (mg)     | -                         | -    | -     | 0.07 | 0.05 | 0.025 | -    | -    | -    |
| Corn syrup (ml)      | -                         | -    | -     | -    | -    | -     | 100  | 90   | 80   |
| Glycerine (ml)       | -                         | -    | -     | 1    | 1    | 1     | 1    | 1    | 1    |
| Orange essence       | q.s.                      | q.s. | q.s.  | q.s. | q.s. | q.s.  | q.s. | q.s. | q.s. |
| Butter               | q.s.                      | q.s. | q.s.  | q.s. | q.s. | q.s.  | q.s. | q.s. | q.s. |

## 2.9. Sterility of the Extract

To ensure the sterility of the *Costus igneus* extract, a sterilization procedure was followed. The extract was filtered using a 0.22 µm sterile filter to remove any microbial contaminants. Additionally, microbiological assays were conducted by inoculating the extract on suitable culture media to check for bacterial and fungal growth. The absence of microbial growth confirmed that the extract was sterile, ensuring its safety for further formulation and use in lollipops [24].

## 2.10. Evaluation parameters [25-31]

### 2.10.1 Physical parameters

Clarity, texture, and consistency, examined through visual inspection. Table 4 presents the pertinent data.

**Table 4.** Physical Appearance of Formulated Lollipops

| F Code | Clarity     | Texture | Consistency    | Stickiness |
|--------|-------------|---------|----------------|------------|
| F1     | Translucent | Smooth  | Slightly Thick | Sticky     |
| F2     | Translucent | Smooth  | Thick          | Non-sticky |
| F3     | Translucent | Smooth  | Thick          | Non-sticky |
| F4     | Translucent | Smooth  | Thick          | Non-sticky |
| F5     | Translucent | Smooth  | Slightly Thick | Sticky     |
| F6     | Translucent | Smooth  | Slightly Thick | Sticky     |
| F7     | Translucent | Smooth  | Thick          | Non-sticky |
| F8     | Translucent | Smooth  | Thick          | Non-sticky |
| F9     | Translucent | Smooth  | Thick          | Non-sticky |

### 2.10.2. Weight variation test

Ten lollipops were weighed individually using an analytical balance. The average weight and standard deviation were calculated to ensure that the weight variation was within prescribed limits: 10% for lollipops ≤ 600 mg, 7.5% for those between 650-750 mg, and 5% for those > 750 mg. The percentage deviation was calculated using the formula:

$$\% \text{ Deviation} = \frac{\text{Individual Weight} - \text{Average Weight}}{\text{Average Weight}} \times 100$$

Table 5 presents the pertinent data.

### 2.10.3. Hardness test

The hardness of the lollipops was measured using a Monsanto Hardness Tester. The crushing strength of ten lollipops was recorded, and the average hardness and standard deviation in kg/cm<sup>2</sup> were reported in Table 6.

### 2.10.4. Moisture content

A 1 g sample of lollipop was weighed and placed in adesiccator for 24 hours. The moisture content was calculated using the formula:

$$\% \text{ Moisture content} = \frac{(\text{Initial weight} - \text{Final weight})}{\text{Initial weight}} \times 100$$

The moisture content is presented in Table 7. **Table 5.** Weight variation of formulated medicated lollipops (N=20)

| S. No. | F Code | Weight of lollipops |
|--------|--------|---------------------|
| 1      | F1     | 4.5035±0.034        |
| 2      | F2     | 4.493±0.039         |
| 3      | F3     | 4.488±0.059         |
| 4      | F4     | 4.515±0.043         |
| 5      | F5     | 4.507±0.030         |
| 6      | F6     | 4.508±0.036         |
| 7      | F7     | 4.518±0.041         |
| 8      | F8     | 4.511±0.038         |
| 9      | F9     | 4.519±0.040         |

**Table 6.** Hardness of Formulated Medicated Lollipops (N=3)

| S. No. | F Code | Hardness of lollipops (Kg/cm <sup>2</sup> ) |
|--------|--------|---------------------------------------------|
| 1      | F1     | 10.5 ±0.57                                  |
| 2      | F2     | 10.75 ±0.94                                 |
| 3      | F3     | 9.7±0.44                                    |
| 4      | F4     | 10.46±0.64                                  |
| 5      | F5     | 10.65±0.57                                  |
| 6      | F6     | 9.65±0.56                                   |
| 7      | F7     | 10.45±0.63                                  |
| 8      | F8     | 10.45±0.43                                  |
| 9      | F9     | 10.50±0.74                                  |

**Table 7.** Moisture Content of Formulated Medicated Lollipops

| S. No. | F Code | Moisture content of lollipops (%) |
|--------|--------|-----------------------------------|
| 1      | F1     | 1.17                              |
| 2      | F2     | 1.00                              |
| 3      | F3     | 0.10                              |
| 4      | F4     | 1.00                              |
| 5      | F5     | 1.10                              |
| 6      | F6     | 0.70                              |
| 7      | F7     | 0.67                              |
| 8      | F8     | 0.73                              |
| 9      | F9     | 0.80                              |

**2.10.5. Drug content uniformity**

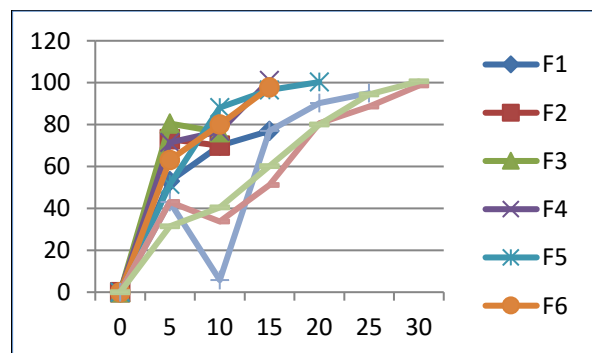
The weight equivalent of one lollipop was dissolved in 50 ml of pH 6.8 phosphate buffer of pH 6.8 in a 100 ml volumetric flask. The volume was made up with buffer, and absorbance was measured at 375 nm using a UV-Visible spectrophotometer. The drug content was assessed to ensure uniformity within 90-110% of the labeled amount. Table 8 presents the pertinent data.

**Table 8.** Percentage Drug Content Uniformity of Formulated Medicated Lollipops

| S. No. | F Code | Drug content (%) |
|--------|--------|------------------|
| 1      | F1     | 58.14±0.30       |
| 2      | F2     | 64.12±3.31       |
| 3      | F3     | 70.68±3.85       |
| 4      | F4     | 72.15±3.5        |
| 5      | F5     | 75.48±0.50       |
| 6      | F6     | 78.59±0.65       |
| 7      | F7     | 73.98±3.50       |
| 8      | F8     | 83.59±0.53       |
| 9      | F9     | 89.96±0.76       |

**2.10.6. In-vitro drug release**

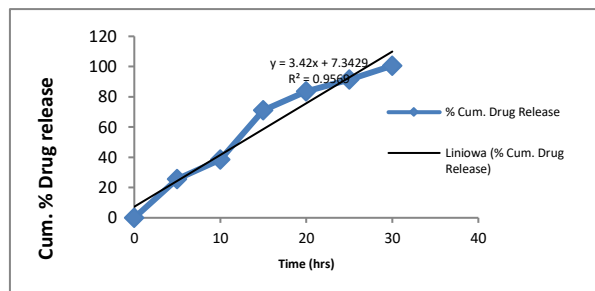
The *in-vitro* drug release was tested using a USP dissolution apparatus type II (paddle). The lollipops were placed in 250 ml of phosphate buffer (pH 6.8) and stirred at 100 rpm. Aliquots of 5 ml were withdrawn at 5-minute intervals, and each sample was analyzed at 375 nm using a UV-Visible spectrophotometer to determine the drug release based on the standard calibration curve. Table 9 presents the pertinent data, while Fig. 7 illustrates it.

**Fig. 7.** In-vitro release profile of the formulations F1 to F9.**2.11. Evaluation of in-vitro release kinetics of optimized formulation**

To evaluate the release kinetics, the data obtained from the drug release study were plotted in various kinetic models.

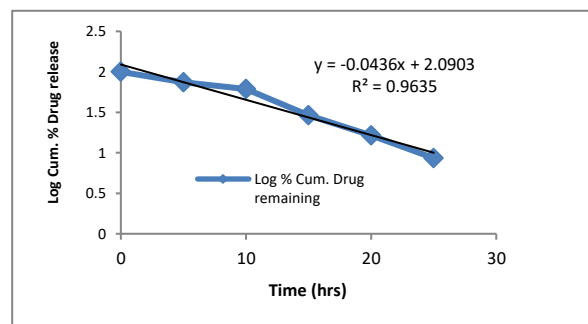
**2.11.1. Zero order equation**

Percentage drug released was plotted against time, and the data were fitted to  $C = K_0t$ , where  $K_0$  is the zero-order constant. A straight line would indicate zero-order release.

**Fig. 8.** Zero order kinetics**2.11.2. First order equation**

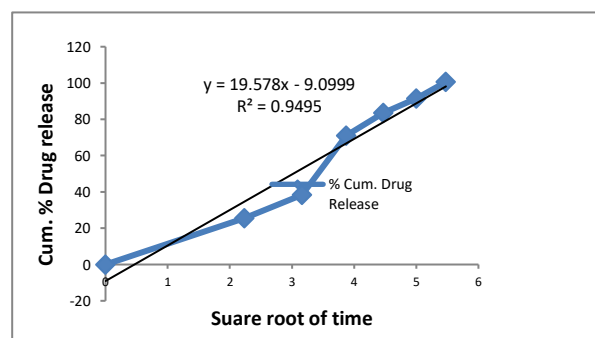
It was reported that the first-order kinetics model can be analyzed by plotting  $\log(\% \text{ cumulative drug remaining})$  versus time. The data was fitted to the equation:

$C = \log C_0 - Kt/2.303$ , where  $C_0$  - initial concentration of drug and  $K$  - first order constant

**Fig. 9.** First order kinetics**2.11.3. Higuchi kinetics**

The Higuchi model was utilized to understand the diffusion-controlled release of the drug. For this, the cumulative drug released was plotted against the square root of time. The data were fitted to the equation:

$Q = Kt^{1/2}$ , where  $K$  is the Higuchi constant. A straight line indicates Higuchi release kinetics.

**Fig.10.** Higuchi kinetics

**Table 9.** In-Vitro Drug Release Study of Medicated Lollipops

| Time (min.) | Percentage Drug Release (%) |      |       |       |       |       |       |       |       |
|-------------|-----------------------------|------|-------|-------|-------|-------|-------|-------|-------|
|             | F1                          | F2   | F3    | F4    | F5    | F6    | F7    | F8    | F9    |
| 0           | 0                           | 0    | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
| 5           | 53                          | 73.0 | 80.5  | 71.5  | 51.5  | 63    | 43    | 43    | 31.4  |
| 10          | 70.0                        | 70.0 | 76.38 | 76.86 | 88.06 | 80.00 | 5.70  | 33.8  | 40.40 |
| 15          | 77.0                        | -    | -     | 101.1 | 96.5  | 97.7  | 77.0  | 51.08 | 60.2  |
| 20          | -                           | -    | -     | -     | 100.3 | -     | 90.3  | 80.6  | 80    |
| 25          | -                           | -    | -     | -     | -     | -     | 95.00 | 88.6  | 94.4  |
| 30          | -                           | -    | -     | -     | -     | -     | -     | 98.6  | 100.6 |

**Table 10.** In-Vitro Release Kinetics Of Optimized Formulation

| Time [min] | Square root of time | Log Time | % Cum. Drug Release | % Cum. Drug Remaining | Log % Cum. Drug remaining | Log % Cum. Drug Release | Cube root of % drug remaining |
|------------|---------------------|----------|---------------------|-----------------------|---------------------------|-------------------------|-------------------------------|
| 0          | 0                   | ∞        | 0                   | 100                   | 0                         | ∞                       | 0.60107                       |
| 5          | 0.03607             | 0.67877  | 05.5                | 70.5                  | 1.87016                   | 1.00650                 | 0.00777                       |
| 10         | 3.16008             | 1        | 38.0                | 61.6                  | 1.78758                   | 1.58033                 | 3.70736                       |
| 10         | 3.87078             | 1.17607  | 71                  | 07                    | 1.0600                    | 1.8536                  | 3.07030                       |
| 00         | 0.0703              | 1.30103  | 83.6                | 16.0                  | 1.0380                    | 1.70001                 | 0.50067                       |
| 05         | 5                   | 1.37770  | 71.0                | 8.6                   | 0.7305                    | 1.76075                 | 0.0088                        |
| 30         | 5.0770              | 1.0773   | 100.6               | -0.6                  | -                         | 0.0006                  | -0.8030                       |

**Table 11.** Evaluation Parameters Post-Stability Studies of Optimized Formulation (F9)

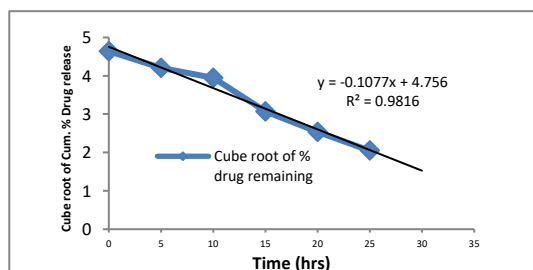
| Evaluation Parameter | Optimized Formulation (F9) | After Stability Study of 1 Month |
|----------------------|----------------------------|----------------------------------|
| Weight variation     | 4.519±0.040                | 3.515±0.58                       |
| Hardness             | 10.50±0.74                 | 10 ±0.08                         |
| Thickness            | 3.44±0.041                 | 3.18±0.16                        |
| Moisture Content     | 0.80%                      | 0.67 %                           |
| Content uniformity   | 89.96%±0.76                | 76.08±1.30                       |
| Drug release         | 100.6%                     | 77.0%                            |

#### 2.11.4. Hixson and Crowell erosion equation

To analyze the release of a drug using the Hixson-Crowell erosion equation, the relationship between the cube root of the percentage of drug remaining over time is modeled by:

$$Q_{01/3} - Q_{t1/3} = KHCXt$$

where KHC is the rate constant.

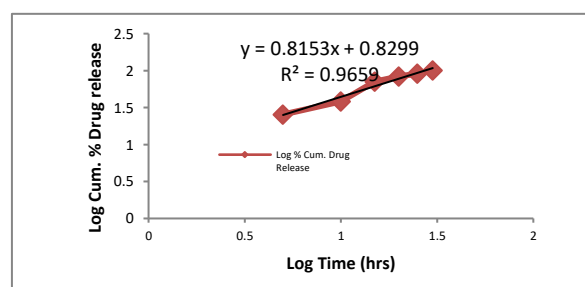
**Fig. 11.** Hixson-Crowell kinetics

#### 2.11.5. Korsmeyer-Peppas equation

For Korsmeyer-Peppas drug release kinetics, the cumulative percentage of drug released is fitted to:  $M_t/M_\infty = Kt^n$ ,  $\log M_t/M_\infty = \log K + n \log t$ , where  $M_t/M_\infty$  is the fraction of drug released, K is the kinetic constant, and n is the diffusional exponent. Interpret n to determine the release mechanism.

If the value is 0.5 or less, the release mechanism follows “Fickian Diffusion” and higher values of  $0.5 < n < 1$  for mass transfer follow a non-fickian model (anomalous transport).

The drug release follows zero-order drug release and casell transport if the value is 1. For the values of n higher than 1, the mechanism of drug release is regarded as super case II transport. This model is used to analyse the release of pharmaceutical polymeric dosage forms when the release mechanism is not known or more than one type of release phenomenon was involved. The n value could be obtained from slope of the plot of long cumulative percentage of drug release vs log time. The results were collected in Table 10, while Fig. 8-12 illustrate them.

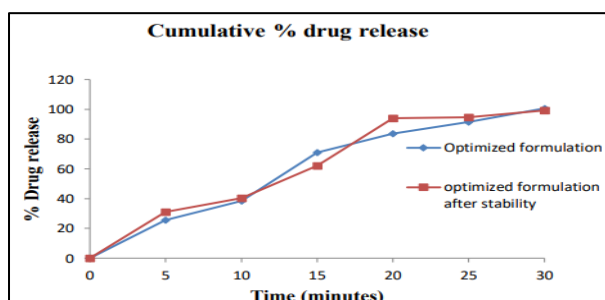
**Fig.12.** Korsmeyer-Peppas kinetics

#### 2.12. Stability studies

The optimized formulations were subjected to



stability studies at 40°C/75% RH for one month to evaluate their stability over time. Table 11 presents the pertinent data, while Fig. 13 illustrates it.



**Fig. 13.** Comparative cumulative percentage drug release profile for pttimized formulation (F9) of *Costus igneus* extract

### 2.13. In-vivo drug release

*In vivo* antidiabetic efficacy of the optimized *Costus igneus* herbal lollipop formulation was evaluated in healthy male Wistar albino rats (160±20 g), following ethical guidelines approved by the Institutional Animal Ethics Committee (protocol number 01/IAEC/VVIPS/2023). The rats were fasted overnight and randomly divided into two groups: Group I received a marketed anti-diabetic formulation (positive control), and Group II was administered the herbal lollipop orally once daily for 28 days. The dosage was based on traditional *Costus igneus* use, adjusted for rat body weight. Blood glucose levels were measured at regular intervals, and statistical analysis was performed using repeated measures ANOVA ( $p < 0.05$ ). This study aimed to compare the antidiabetic effects of the herbal formulation with a known treatment. Future studies with larger sample sizes and additional experimental groups are recommended for further validation.

## 3. Results

The study involved the preparation and evaluation of *Costus igneus* extracts, quercetin medicated lollipops, and their subsequent *in-vitro* and *in-vivo* performance.

### 3.1. Collection and preparation of *Costus igneus* extract

Fresh *Costus igneus* leaves were processed by washing, drying, and grinding them into a powder. Soxhlet extraction using ethanol yielded a concentrated extract.

### 3.2. Determination of quercetin properties

The melting point of quercetin was assessed using an electrical melting point apparatus with the capillary method. The  $\lambda_{\max}$  of quercetin was determined by

preparing a 2000 ppm methanol solution and scanning it from 400-800 nm. The UV spectrum is depicted in Fig. 1.

### 3.3. Drug-excipient compatibility studies

FTIR spectroscopy was used to analyze compatibility between quercetin and various excipients. The FTIR spectra showed characteristic peaks corresponding to functional groups such as OH, phenol, and aromatic ring structures (Table 1 and Fig. 2-4).

### 3.4. Preparation of calibration curve for quercetin

A calibration curve was created by diluting a quercetin stock solution and measuring absorbance at 375 nm. The resulting data (Table 2 and Fig. 5) demonstrated a linear relationship between concentration and absorbance.

### 3.5. Quantitative chemical tests of *Costus igneus* extract

Various tests confirmed the presence of tannins, flavonoids, terpenoids, alkaloids, steroids, and anthocyanosides in the *Costus igneus*. The extract tested negative for saponins and reducing sugars.

### 3.6. Methodology for herbal lollipops

Medicated lollipops were formulated with varying compositions of quercetin, stevia, acacia gum, xanthan gum, corn syrup, glycerine, orange essence, and butter (Table 3 and Fig. 6). Physical parameters including clarity, texture, consistency, and stickiness were evaluated, with the results summarized in Table 4.

### 3.7. Evaluation of parameters

Weight variation, hardness, moisture content, and drug content uniformity of the lollipops were assessed. Results showed that the lollipops met the prescribed limits for weight variation (Table 5), hardness (Table 6), and moisture content (Table 7). Drug content uniformity was measured and is presented in Table 8.

### 3.8. In-vitro drug release

Using USP dissolution apparatus, the percentage of drug release was monitored over time (Table 9 and Fig. 7). The release profile varied among different formulations.

### 3.9. In-vivo drug release

The *in-vivo* study involved administering the lollipops to fasted male Wistar rats and monitoring blood glucose levels over time (Table 12). Data indicated a significant reduction in glucose levels in rats administered the optimized formulation compared to the diabetic control, though less effective than the glibenclamide control.

**Table 12.** In-Vivo Pharmacokinetic Data - Blood Glucose Levels Post-Administration

| Treatment                     | Blood glucose level mg/dl |                |                 |                |                |
|-------------------------------|---------------------------|----------------|-----------------|----------------|----------------|
|                               | Basal value (0hr)         | 1 hr           | 3 hr            | 5 hr           | 7hr            |
| Normal control (vehicle only) | 80.00±1.693               | 80.83±1.721    | 80.83±1.424     | 79.83±1.376    | 78.56±1.254    |
| Diabetic control              | 322.33±7.775              | 327.50±7.945   | 329.50±7.388    | 336.67±6.515   | 345.21±5.427   |
| Glibenclamide 600 µg/kg       | 277.33±7.923              | 206.66±6.280** | 174±7.095**     | 154.83±5.043** | 131.51±3.015** |
| Lollipops                     | 360.21±12.751             | 280±16.241**   | 241.16±16.342** | 232±15.189*    | 270±15.189ns   |

**Glibenclamide 600 µg/kg and Lollipop Treatment** were administered at 600 µg/kg/day for 7 days. All values are expressed as means ± SEM (N=6). Statistical significance is indicated by \*\*P<0.05 for \* and P<0.01 for \*\*. "ns" indicates not significant. **P<0.01 vs Diabetic Control (ANOVA)**

#### 4. Discussion

This study successfully developed medicated lollipops using *Costus igneus* extract, with quercetin and other bioactive compounds showing promising therapeutic potential for diabetes management. The melting point and λ<sub>max</sub> values of quercetin confirmed its purity and identity, consistent with expected values. The formulation process revealed that glycerine as a plasticizer and corn syrup as a binder significantly improved the lollipop's texture, ensuring both palatability and physical stability.

The physical compatibility study confirmed that the drug and excipients had no significant interaction, supporting the formulation's stability. FT-IR spectroscopy showed no chemical changes, aligning with standard practices in excipient-drug compatibility studies. The in-vitro drug release study showed rapid release, with the formulation F9 achieving 100.6% release in 30 minutes. The first-order release kinetic and diffusion-controlled release suggests that the formulation provides quick therapeutic action, which is critical for diabetes management.

In-vivo studies demonstrated a significant reduction in blood glucose levels in diabetic rats, supporting *Costus igneus*'s anti-diabetic properties. These findings suggest that medicated lollipops may offer an alternative to traditional oral dosage forms, improving patient compliance and comfort.

Future research should focus on clinical trials to assess the safety, efficacy, and pharmacokinetics of these lollipops in humans. Further studies could explore sustained-release formulations and combinations with other anti-diabetic agents to enhance efficacy. Overall, this study supports the potential of candy-based medicated lollipops as an innovative and effective alternative for diabetes management.

#### 5. Conclusions

In this study, a novel medicated lollipop formulation containing *Costus igneus* extract was developed and thoroughly evaluated for its potential as an alternative oral dosage form for managing diabetes. The formulations demonstrated physical and chemical stability, with optimal values for hardness, moisture content, and drug release profiles. The use of glycerine as a plasticizer and corn syrup as a binder facilitated the creation of lollipops with favorable texture and appearance. The in-vitro drug release profile showed rapid and substantial drug release, while the in-vivo studies revealed a significant reduction in blood glucose levels in diabetic rats, suggesting the extract's efficacy in glycemic control.

This formulation offers several advantages over traditional oral drug delivery systems, including ease of administration and improved patient compliance, particularly for pediatric and geriatric populations. The promising results of this study suggest that medicated lollipops could be a viable and patient-friendly alternative for diabetes treatment. Future studies should focus on clinical trials to further assess the pharmacokinetics, safety, and long-term therapeutic efficacy of this innovative dosage form. Additionally, exploring the incorporation of

other active pharmaceutical ingredients in lollipop formulations may provide enhanced therapeutic benefits and broaden their applicability in other disease conditions.

**Author Contributions:** Saidatri A: Conceptualization, Original Draft; Lakshmana Rao A: Data Collection, Analysis; Vinod Kumar V.L: Visualization, Supervision; Abhiram Y.V: Funding Acquisition, Resources; Veena Sree P: Writing, Project Administration; Devika M: Writing, Project Administration; Rama Krishna T.P: Review, Editing.

**Funding:** This research received no external funding.

**Acknowledgments:** The authors would like to acknowledge V. V. Institute of Pharmaceutical Sciences, Gudlavaluru.

**Conflicts of Interest:** The authors declare no conflict of interest.

#### References

- Shinde, S. P.; Kondhalkar, S. M. A review on insulin plant (*Costus igneus* L.) and its remedial approaches. *Asian J. Res. Bot.* **2025**, *8*(1), 14-21. DOI: 10.9734/ajrib/2025/v8i1238
- Athilli, L.; Siddiqui, A. F.; Hussain, F.; Parvez, E. A. H. Pharmacognostic study and pharmacological potentials of *Costus igneus* plant - Review. *Int. J. Pharmacogn.* **2021**, *8*(12), 476-486. DOI: 10.13040/IJPSR.0975-8232.IJP.8(12).476-86
- Laha, S.; Paul, S. *Costus igneus* - A therapeutic anti-diabetic herb with active phytoconstituents. *Int. J. Pharm. Sci. Res.* **2019**, *10*(8), 3583-3591. DOI: 10.13040/IJPSR.0975-8232.10(8).3583-91
- Shubham, K.; Mittal, A.; Babu, D.; Mittal, A. Herbal medicines for diabetes management and its secondary complications. *Curr. Diabetes Rev.* **2021**, *17*(4), 437-456. DOI: 10.2174/1573399816666201103143225
- Azhagu Madhavan, S.; Ganesan, S.; Sripriya, R.; Priyadharshini, R. A literature review of anti-diabetic medicinal plant properties (*Costus* species). *J. Biomed. Res. Environ. Sci.* **2021**, *2*(5), 305-310. DOI: 10.37871/jbres1231
- Khandale, S. N.; Sonavane, M. Potential therapeutic efficacy of *Costus igneus* for diabetes mellitus & other diseases with framework for its evaluation based on Ayurveda. *Int. J. Adv. Res.* **2019**, *7*(12), 813-818. DOI: 10.21474/IJAR01/10215
- Shivaprakash, G.; Thottacherry, E. D.; Rai, S.; Nandini, M.; Kumarachandra, R. Evaluation of antioxidant potential of *Costus igneus* in ethanol induced peroxidative damage in albino rats. *J. Appl. Pharm. Sci.* **2014**, *4*(8), 052-055. DOI: 10.7324/JAPS.2014.40810
- Vinotha, V.; Iswarya, A.; Thaya, R.; Govindarajan, M.; Alharbi, N. S.; Kadaikunnan, S.; et al. Synthesis of ZnO nanoparticles using insulin-rich leaf extract: Anti-



- diabetic, antibiofilm and antioxidant properties. *J. Photochem. Photobiol. B: Biol.* **2019**, 197, Art. No: 111541. DOI: 10.1016/j.jphotobiol.2019.111541
9. Talasila, E. G. K.; Bavirsetti, H.; Chimakurthy, J.; Candasamy, M. Effect of *Costus igneus*: The insulin plant, on pre-diabetes and diabetes in neonatal streptozotocin rats. *J. Health Sci.* **2014**, 4(3), 162-168. DOI: 10.17532/jhsci.2014.163
10. Chandrakar, N.; Kaur, J.; Banerjee, M. Synergies of bioactivities, mechanisms, dietary factors and functional food applications of medicinal insulin plant (*Costus pictus* D.): A review. *Int. J. Food Sci. Technol.* **2024**, 59, 8933-8942. DOI: 10.1111/ijfs.17588
11. Josephine, I. G.; Punngai, K. In vitro cytotoxicity activity of ethanolic leaf extract of *Costus igneus* against hepatocellular carcinoma (HepG2) cells. *Biomed. Pharmacol. J.* **2024**, 17, Art. No: 1715. DOI: 10.13005/bpj/1715
12. Dhoni, P. G.; Goyal, M.; Sahu, Y. P.; Mubeen, M. F. To evaluate antioxidant activity of *Costus igneus* in ethanol induced peroxidative damage in albino rats. *Int. J. Health Sci.* **2022**, 6(S5), Art. No: 9858. DOI: 10.53730/ijhs.v6n5.9858
13. Ratnakar, S. M.; Prakash S. B. Phytochemical analysis of different solvent extracts of *Costus igneus*. *Int. J. Food Nutr. Sci.* **2022**, 11(12), 2364-2368
14. Jadhav, G.; Pagire, D.; Jadhav, V. Formulation and evaluation of anti-diabetic tablet from insulin plant (*Costus igneus*). *Int. J. Multidiscip. Res.* **2023**, 5(3), Art. No: IJFMR23032976
15. Prabhu, P. P.; Malli, R.; Koland, M.; Vijaynarayana, K.; D'Souza, U.; Harish, N. M.; Shastri, C. S.; Charyulu, R. N. Formulation and evaluation of fast dissolving films of levocetirizine dihydrochloride. *Int. J. Pharm. Invest.* **2011**, 1(2), 99-104. DOI: 10.4103/2230-973X.82417
16. Jacob, S.; Boddu, S. H. S.; Bhandare, R.; Shabbir, S. Orodispersible films: Current innovations and emerging trends. *Pharmaceutics* **2023**, 15(12), Art. No: 2753. DOI: 10.3390/pharmaceutics15122753
17. Alburyhi, M. M.; Noman, M. A.; Saif, A. A.; Mohamed, Y. A. S.; Hamidaddin, M. A.; Yahya, T. A. A.; Al-Ghorafi, M. A.; Abdullah, J. H. Lisinopril-excipient compatibility studies for advanced drug delivery systems development. *World J. Pharm. Res.* **2024**, 13(16), 59-111. DOI: 10.20959/wjpr202416-33678
18. Singh, C.; Rao, K.; Yadav, N.; Bansal, N.; Vashist, Y.; Kumari, S.; Chugh, P. A review: Drug-excipient incompatibility by FTIR spectroscopy. *Curr. Pharm. Anal.* **2023**, 19(5), 371-378. DOI: 10.2174/1573412919666230228102158
19. Alburyhi, M. M.; Noman, M. A.; Saif, A. A.; Hamidaddin, M. A.; Yahya, T.A.A.; Abd-hafiz Al-Ghorafi, M.A. Rosuvastatin-excipient compatibility studies for advanced drug delivery systems development. *World J. Pharm. Res.* **2024**, 13(13), 1549-1582. DOI: 10.20959/wjpr202413-33126
20. Vijaya, V.; Karunai Selvi, B. K.; Arockia John, P.J.; Ramya, S.; Jayakumararaj, R. Phytochemical screening, GC-MS and FTIR analysis of bioactive compounds in methanolic leaf extracts of *Costus igneus* (CIMLE) as a natural source of drug lead molecules for next-generation drug-design, development and therapeutics. *J. Drug Deliv. Ther.* **2022**, 12(5-S), 142-155. DOI: 10.22270/jddt.v12i5-s.5658
21. Muthukumar, C.; Cathrine, L.; Gurupriya, S. Qualitative and quantitative phytochemical analysis of *Costus igneus* leaf extract. *J. Pharmacogn. Phytochem.* **2019**, 8(4), 1595-1598.
22. Bharathi, J. K.; Prakash, M. A. S. Phytochemical screening and quantitative analysis, FTIR and GC-MS analysis of *Costus pictus* D. Don ex Lindl. leaf extracts - A potential therapeutic herb. *J. Indian Chem. Soc.* **2024**, 101(11), Art. No: 101362. DOI: 10.1016/j.jics.2024.101362
23. Khandagale Sandip Suresh, Mahalkar Ram Babasaheb, Madane Somnath Jotiram, Patil Onkar Ganpat, Dabhade Sakshi kailasrao, Salve Dvitiya Shantilal. To study the preparation, formulation and evaluation of medicated lollipop. *Int. J. Pharm. Sci.* **2024**, 2(5), 1275-1291. DOI: 10.5281/zenodo.11264459
24. Rao, N. B.; Gajula, R. G.; Sujatha, E.; Kumari, O. S. Phytochemical analysis and anti-microbial activity of *Costus igneus* (insulin plant) leaf extract. *Int. J. Biol. Pharm. Allied Sci.* **2016**, 5(6), 1207-1214.
25. Bedse, A.; Nalawade, A.; Dhamane, S.; Kachave, R. N.; Wagh, V.; Tare, H.; Ghangale, G. Formulation and evaluation of herbal remedy for cough. *Int. J. Pharm. Qual. Assur.* **2023**, 14(3), 762-766. DOI: 10.25258/ijpqa.14.3.51.
26. Cunha, F. A. B.; Matias, E. F. F.; Brito, S. V.; Ferreira, F. S.; Braga, J. M. A.; Costa, J. G. M.; Coutinho, H. D. M. Phytochemical screening, antibacterial activity and in vitro interactions between *Costus cf. arabicus* L. with UV-A and aminoglycosides. *Nat. Prod. Res.* **2012**, 26(4), 380-386. DOI: 10.1080/14786419.2010.545776.
27. Sahoo, M. R.; Srinivasan, U. M.; Varier, R. R. Development and evaluation of Talisapatradi and Vyoshadi Choorna lozenges—An Ayurvedic traditional formulation. *J. Rep. Pharm. Sci.* **2022**, 11(1), 110-117. DOI: 10.4103/jrtps.JRTPS\_80\_21.
28. Chowdary, A. R.; Raaththika, R.; Vijayalakshmi, P. Evaluation of the cookies formulated with *Costus igneus* plant material for antidiabetic activity. *Medico-Legal Update* **2020**, 20(3), 265-271.
29. Choppala, P. B.; Gera, V. N.; Inakoti, R. K.; Malakondaiah, G. *Costus igneus* oro-herbal films: Innovative and cost-effective therapy. *Int. J. Food Nutr. Sci.* **2022**, 11(11), 3962-3974.
30. Ding, Y.; Chu, N.-n.; Wang, R.; Qin, W.; Shi, Y.-f.; Qian, Z.-z.; Liu, B.; He, Q. Pharmacokinetic and pharmacodynamic evaluation study of etomidate: a randomized, open-label, 2-period crossover study in healthy Chinese subjects. *Sci. Rep.* **2024**, 14, Art. No: 7071. DOI: 10.1038/s41598-024-57581-2.
31. Hock, F. J.; Gralinski, M. R. (Eds.). *Drug Discovery and Evaluation: Methods in Clinical Pharmacology, Living Reference Work*; Springer Nature: **2020**.