

Fabrication and Preliminary Assessment of Neem Fruit Mucilage as Mucoadhesive Abetting Assets with Methpol-934P for Acyclovir Delivery from Mucoadhesive Microcapsules

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In this study, we investigated the mucoadhesive properties of neem fruit mucilage by incorporating it into mucoadhesive microcapsules with Acyclovir (ACR). Methpol-934P and Neem fruit mucilage (NFM) was used to construct 12 different mucoadhesive microcapsules. We assessed FTIR and DSC capabilities for compatibility with ACR and NFM. ACR mucoadhesive microcapsules (ANMM) were characterized for mucoadhesion and ACR release Physico-chemical characteristics. CR was found to be compatible with NFM in the research. The entrapment increased as the levels of NFM in the formulations increased, and mucoadhesion time was longer in formulations with higher levels of NFM. As levels of NFM increase in formulations, the release of drugs is slightly reduced. NFM may be responsible for this due to its release retarding properties. An additive of neem fruit mucilage allowed for the retention of ACR after ingestion when a mucoadhesive polymer (methpol 934P) was used.

Keywords: Acyclovir; anti-viral; Mucoadhesive; Microcapsules; Neem.

A unique attitude is emerging for drug administration to increase the gastric availability of drugs with patient consent. Among the various dosage forms, gastro retentive microcapsules are of special concern as they can be easily prepared and administered^{1, 2}.

Herpes simplex, herpes zoster, and chicken pox are all contagions treated with acyclovir, a purine nucleoside analogue^{3, 4}. Approximately 15-30% of Acyclovir is bioavailable orally. Acyclovir

has a half-life⁵ of ~2 h. After giving the medication orally, the medication is well absorbed into the stomach.

A mucoadhesive system's effectiveness is significantly affected by the polymer used. Many patients prefer oral drug administration due to its convenience. Many polymers have been tried for mucoadhesive drives, which are rare and expensive. An ideal polymer would aid mucoadhesion and be derived from nature. The authors plan to examine

mucoadhesive microcapsules using neem fruit mucilage (NFM). The antiviral properties of NFM have been demonstrated in studies^{6,7}. NFM may be helpful in antiviral therapy. In expanded time, ANMM aims to achieve steady-state availability. As they are designed for ease, precision liberation systems are an effective solution for short-acting drugs and those that require incessant medicating.

MATERIALS AND METHODS

Materials

Acyclovir (ACR) was from Innovative Pharmaceuticals, Hyderabad, Telangana. Methpol 934P, and dichloromethane were from Merck, Hyderabad.

Extraction of mucilage

Depletion of expression was defined⁸ by Ahad *et al.*, 2021. After washing and removing the outer layer of the neem fruits, they were soaked in water, boiled for an hour, and cooled. The seeds were separated by using ethyl acetate, butanol, and petroleum ether (50%). Using a multilayered muslin cloth bag, the marc was extracted from the mucilage. The mucilage was parted, parched in an oven (ACM-22066) at 40°C, poised, ground, allowed to pass over a # 80 sieve (MSW Labs) and stored in a desiccator (Tarson 402020) at 30°C and 45% RH.

Cleansing of the Mucilage

The NFM was homogenised (APV-1000) with 5% trichloroacetic acid, centrifuged (Systonic S-103), neutralized with NaOH, and dialyzed (SpectraFlo) neutralized with distilled water, as defined by Hindustan *et al.* 2009. As the last step, ethanol (95%) was treated with the precipitate and scrubbed with acetone⁹.

Preparation of ANMM

Dichloromethane and acetic acid (2% v/v) were used in the blending of Methpol 934P, ACR, EC, and NFM. Continuous stirring of this mixture into liquid paraffin (containing span 80) was achieved using a three-bladed propeller stirrer (IKA-R1381). We added glutaraldehyde at a rate of 4 drops per minute dropwise to the sample as part of this procedure. Three hours of stirring followed. To remove liquid paraffin, the Acyclovir-Neem mucoadhesive microcapsules (ANMM) were centrifuged and washed with petroleum ether. For

the removal of residual glutaraldehyde, an ANMM was suspended in a 5% sodium bisulfite solution for 15 min. After washing with distilled water, the last step was to dry the clothes. Desiccators were used to dry and store the ANMM¹⁰⁻¹².

Evaluation parameters

Drug excipient compatibility studies

DSC studies

In a mini pan of DSC, ACR and NFM were mixed in a 1:1 ratio (10 mg) and scanned from 50 to 300°C (Venchal Scientific-412105-USA).

FTIR studies

ACR and NFM were examined using FTIR spectroscopy (Bruker) by scanning at a 4000-400 cm⁻¹ array.

Evaluation of physical properties

Measurement of particle size

ANMM particles were measured using a stage micrometer. Dry ANMM were measured with an eyepiece micrometre on a hygienic glass slide¹³. At least 100 ANMM were counted per batch.

Production yield

In each of the three trials, the average weight of parched ANMM (W_1) recovered from each trial was compared¹⁴ to the total of the initial dry weight (W_2).

$$\% \text{Percentage Yield} = \frac{\text{Weight of attained by microcapsules}}{\text{Total weight of drug and polymeric}} \times 100$$

Entrapment Efficiency

100 mg of ANMM were dispersed in 0.1 M HCl overnight with erratic quivering. The mixture was filtered at 254 nm, and the filtrate was analyzed spectrophotometrically (Elico Spectrophotometer, SL-174). An evaluation of entrapment efficiency was based on the ratio between the actual amount of drug in the formulation and the amount initially added¹⁵.

$$\text{Entrapment efficacy} = \frac{\text{Practical drug yield}}{\text{Theoretical drug content}} \times 100$$

Measurement of swelling

An HCl solution of 0.1M was used to swell ANMM. As determined from the following equation¹⁶, the weight gain was determined by the difference between the weight gained at time t (X_t) and the beginning time ($t = 0$ [X_0]).

RESULTS AND DISCUSSION

In addition to evaluating the congeniality of the fresh NFM, its colour was yellowish green, which assists ANMM.

Compatibility studies

Based on the DSC assessment, the pure ACR produced a sharp endothermic peak, indicating its purity. Combining this peak with left-shifting excipients broadens it. DSC observations indicate that ACR does not interact with the excipients.

The ACR pure-form spectrum exhibits FTIR bands for secondary amines, phenyl esters, and carboxylic groups. Blend (F-5) had peaks and stretches like pure drugs. Excipients did not obstruct peaks or stretches of the spectrum of ACR.

Physical properties

Particle size

Optical microscopy was used to fix particle size for all formulations. ANMM array sizes range from 33.92 ± 0.7 to 39.6 ± 0.8 μm (Figure 1), with F-8 having the largest particle size.

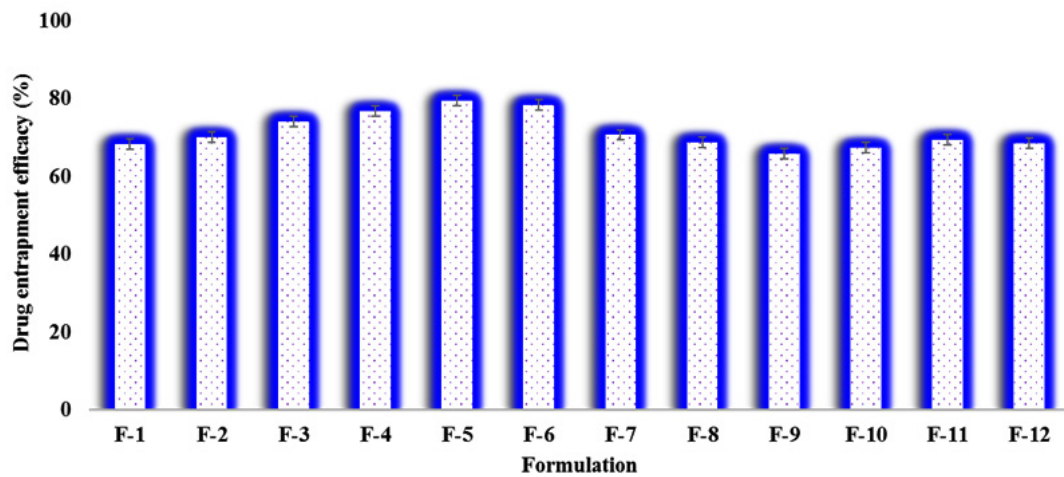


Fig. 2. Drug entrapment efficacy of ANMM

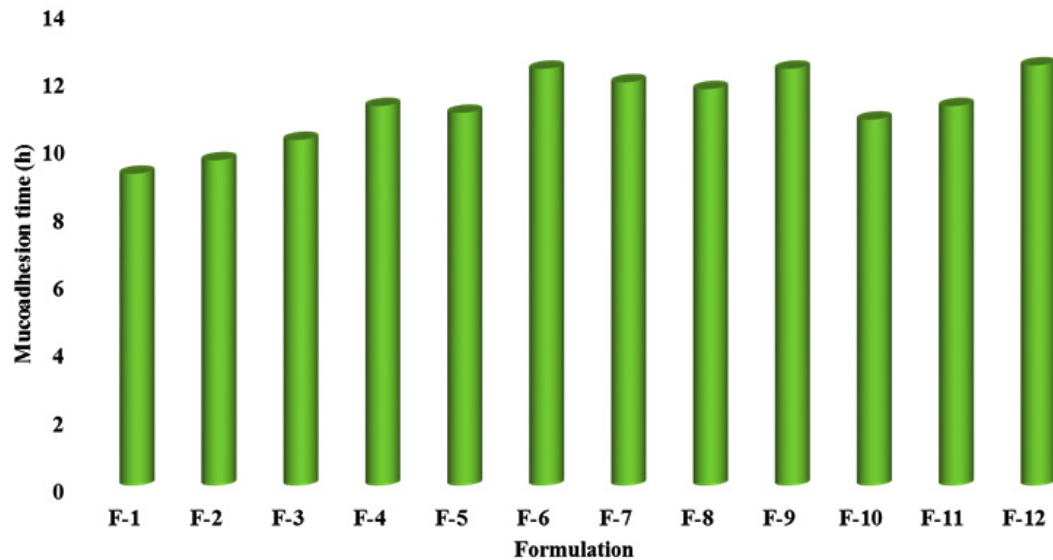


Fig. 3. Mucoadhesive time of ANMM

Yield of ANMM

ANMM yielded 80.5±2.3 to 94.4±1.7, with F-2 to F-6 showing a maximum (Figure 1).

In vitro drug release

Analyses were conducted to determine whether ANMM dissolves. As NFM shows more binding properties and releases retarding properties, formulations with 50 to 100 mg of NFM show good drug release, whereas formulations with F-5 to F-12 show suppressed drug release.

Swelling Measurement

By analyzing the pattern of ACR release, the ANMM can be used to determine the extent of mucoadhesion. When preparing any mucoadhesive formulation, this study should be considered. Different concentrations of NFM were tested on the swelling indices of the ANMM. The swelling index dropped steadily as the concentration of NFM decreased, and batch F-12 was the most swollen. Several polar compounds are present in NFM, which enable it to absorb and hold water, as well as have swelling assets.

% Drug entrapment

Entrapment of ANMM ranged from 65.9±1.27 to 79.6±0.98 and formulations with 125mg of NFM gave good entrapment of ACR (Figure 2).

In vitro mucoadhesion time

All batches of ANMM had mucoadhesions ranging from 9.2±0.08g (F-1) to 12.4±0.16g (F-12) (Figure 3). The mucoadhesion time was considered to increase with a higher NFM content and higher levels of methpol 934 P.

ACR estimation

A UV-VIS spectrometer was used to obtain a calibration curve for ACR estimation in 0.1M HCl solution at 254 nm ϵ_{\max} . According to Beer's law, the calibration curve ranged from 0-10 µg/ml (repeated three times). Such data can be used to determine the uniformity of content.

CONCLUSION

Acyclovir (ACR) is released from mucoadhesive polymers at a rate and quantity controlled by the polymers. The ACR is released from the stomach after the microcapsules are digested. To formulate ACR, Neem (*Azadirachta indica*) fruit mucilage (NFM) combined with methpol 934 P was used. NFM was proven to

have antiviral activity in addition to mucoadhesive assets. As earlier studied by Shiraki *et al.*, 2021. Compared to other formulations, F-2 to F-4 with fewer NFM (50 to 100 mg) has more entrapped ACR in addition to the mucoadhesion. An additional increase in NFM retards the ACR release and shows sustained release unlike it was observed by Ghumman *et al.*, 2020. Using the results of this study, it can be concluded that the mucoadhesive microcapsules of ACR with NFM aided by methpol 934 P are an effective way to retain the stomach and support increased bioavailability.

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Conflict of Interests

The authors declare no conflict of interest.

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