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Research Article

Release profile of encapsulated microparticles based on *Landolphia owariensis* (Apocynaceae) extract contained in suppositories for the treatment of hemorrhoidal crisis

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Abstract

Introduction: Hemorrhoidal disease is one of the most frequent causes of anal complaints. The general aim of this study was to evaluate the release profile of the encapsulated drug, in order to overcome the limitations of conventional galenic forms, while maintaining their efficacy.

Methods: Determination of the active ingredient contained in *Landolphia owariensis* extract was carried out by UV-Visible spectrophotometry. Release studies were carried out in a continuous flow cell. The dissolution profile of the suppository containing microparticles was compared to the dissolution profile of suppositories containing the unencapsulated extract and to that of *Landolphia owariensis* extract-based microparticles.

Results: The percentage of active ingredient released from suppositories containing microparticles and those containing the extract alone was 69.47% and 80.01% respectively. Flavonoid release from suppositories containing microparticles was slower, with a release rate of 6.31µg/mm, slightly close to the release rate of extract based microparticles (7.37µg/mn); in contrast, in vitro flavonoid release from suppositories containing the extract was faster (19.85µg/mm).

Conclusion: Release trials have shown the influence of the sodium alginate matrix system on PA release kinetics. These innovative suppositories will help improve compliance and the treatment of hemorrhoidal crisis.

Keywords: Microparticles, Suppositories, *Landolphia owariensis*, Hemorrhoids, In vitro release.

INTRODUCTION

Hemorrhoidal disease is nowadays a crucial phenomenon affecting many people, even if the majority of attacks are non-emergency. [1,2]. Hemorrhoids are complex vascular formations in the anal region. These formations are normally present in all individuals from birth. The term "hemorrhoid" is often misused to refer to hemorrhoidal disease.

Today, hemorrhoidal disease is one of the most common causes of anal complaints, according to a 2012 study. [3] . Hemorrhoidal disease can be treated in a number of ways, including surgery, medication and instruments.

However, in our country, the treatment of haemorrhoidal crises has always been a matter for traditional practitioners. [4]

Several plants are used in the therapeutic arsenal for hemorrhoidal crises, including *Landolphia owariensis p. Beauv* (Apocynaceae), a climbing plant species. The liana bark of this plant is used to treat hemorrhoidal crises in the form of a decoction for internal hemorrhoids and a sitz bath for external hemorrhoids.

This plant, which is a well-known component of the flora of many African countries, contains numerous active substances including quercetin (flavonoids), gallic acid (polyphenol) (Fofana et al., 2020). [5] . Its interest in the treatment of haemorrhoidal crisis has led to phytochemical and pharmacological research.

Indeed, recent studies have revealed that the plant has both a preventive and curative effect on hemorrhoidal disease in decoctate form. [6]. The aim is to obtain a sustained- release form based on the extract, thus improving compliance and the treatment of hemorrhoidal crisis.

Microencapsulation of the active ingredient will enable prolonged or sustained release of the encapsulated drug. [7]

In this work, the aim is to evaluate the release profile of the encapsulated drug in order to overcome the limitations of conventional galenic forms, while maintaining their efficacy.

MATERIALS

The raw materials used were as follows: *Landolphia owariensis* (Apocynaceae) microparticles, Osmotic water; Potassium di-hydrogen phosphate (KH_2PO_4) LOT n°0000510211 / Applichem Gmbh and Sodium hydroxide (NaOH) LOT

:1866402/ Fisher Chemical.

METHODS

1. Study of release kinetics:

1.1 Dosage of active ingredient in *Landolphia owariensis* extract

UV-Visible spectrophotometry has been used to characterize the release of encapsulated PA; this requires determination of the calibration curve and knowledge of the wavelength for maximum absorption of the extract. [8]

Principle of UV-Visible spectrophotometry

Molecular absorption in the ultraviolet (UV) and visible spectrum depends on the electronic structure of the molecule. Energy absorption is quantified and results from the transition of electrons from ground-state orbitals to higher-energy excited-state orbitals. [8]

A more appropriate expression of absorption intensity is that derived from Beer-Lambert's law, which establishes the relationship between absorbance, sample thickness and the concentration of absorbing species.

This relationship is written : **A= log (I0 /I) = å bC equation 5**

With:

A: Absorbance or optical density;

I0 : Intensity of the irradiation energy arriving on the sample;

I: Intensity of the radiation passing through the sample;

å: Characteristic constant of the solute (molecular absorption or molar extinction coefficient: mol-1. l. cm-1);

b : Optical path length through the sample (cm);

C: Solute concentration (mol. L-1).

Determining the wavelength for maximum extract absorption

UV-visible adsorption spectra of the extract were determined. The absorbance (**A**) or optical density (**OD)** is defined as A = OD = log(I0 /I), where **I0** represents the incident intensity and **I** the transmitted intensity.

The absorbance of the stock solution is determined by scanning for wavelengths between 200 and 700 nm. The wavelength marking the concentration peak was recorded.

Preparing the stock solution

The stock solution was prepared as follows: Weigh out 100 mg of the extract; Place the extract in a 100 ml flask; Add osmosis water up to the mark and dissolve the extract in the osmosis water under stirring until the extract is completely dissolved.

Determining the calibration line

Dilutions of the stock solution were made to determine the calibration range (10th, 20th, 25th, 50th, 100th, 150th, 250th, 500th dilutions).

How it works

Prepare the solutions for my calibration range; Fill the quartz cuvette with the solution; Use the same cuvette for the sample and for the blank; Measure the absorbance of the blank (RO water) as well as for each solution, using the extract's wavelength of maximum absorption; - Draw the calibration curve from the average of the readings obtained with the different solutions; Determine the concentration of PA in the solution to be examined using the curve obtained.

2. Dissolution tests

Preparation of the dissolving medium

According to the American Pharmacopoeia (USP), the dissolution medium is a Phosphate Buffer Medium pH 6.8: Dissolve 6.8 g of KH2PO4 in one liter of distilled water, then adjust the pH of the prepared solution to 6.8 using a 1M NaOH solution. [9]

Dissolution test

The test was carried out on the continuous flow cell. Set the dissolution speed according to the ejection rate of the dissolution medium; Insert a fictitious membrane between chamber A and chamber B; the membrane was a circular piece of porous filter paper (PRAD DUMAS, France) 2.4 cm in diameter. Place 1 suppository in chamber A (donor); Heat the dissolving medium to an appropriate T° depending on the Tƒ of the suppository; Suction of the dissolving medium by the pump; Passage through chamber A of a continuous flow at constant flow rate; Dissolution of the PA and passage into chamber B; Ascent to the filtration cell where debris will be retained and finally Passage of the PA into the filtrate collected by a collecting beaker.

The release test was carried out over a period of 6 h, with 1 ml of solution taken from the collection beaker at t0 and then every 30 min until total dissolution.

Samples were assayed at the end of manipulation. The concentration of PA released was assessed by UV-visible spectrophotometry, and the reading was taken at the extract's maximum absorption length. The results of the release tests were expressed as the percentage of active ingredient released as a function of **time [10].**

Two release tests were carried out, and the dissolution profile of the suppository containing microparticles was compared with the dissolution profile of suppositories containing the unencapsulated extract.

RESULTS

STUDY OF LIBERATION KINETICS

Dosage of active ingredient

Determining the wavelength for maximum absorption of extract

Peak concentration was measured at 245 nm.

Determination of extract calibration line

The absorbance values of the standards: daughter solutions assayed using a UV-visible spectrophotometer at 245 nm are shown in Table **I**.

Table I: Absorbance of standards as a function of concentration

Concentration	0	0.002	0.004	0.0067	0.01	0.02	0.04	0.05	0.1
Absorbance	0	0.004	0.011	0.043	0.065	0.164	0.308	0.376	0.713

The calibration curve obtained is shown in **Figure 2** below. According to the calibration curve, the equation of the straight line is: Abs = 7.3081 * C - 0.0021

Release test for the active ingredient in formulated suppositories

Flavonoid release profile

Flavonoid release tests were carried out on suppositories containing the microparticles, on suppositories containing the simple extract and on extract-based microparticles. The aim was to assess the release profile of the encapsulated active ingredient.

Cumulative masses and dissolved fractions were determined for each sample.

The results enabled us to plot the release profiles of total flavonoids from suppositories containing the microparticles, (see figure 2), also to plot the flavonoid dissolution profile (figure 3) of suppositories containing the extract and to plot the flavonoid dissolution profile from the microparticles (figure 4).

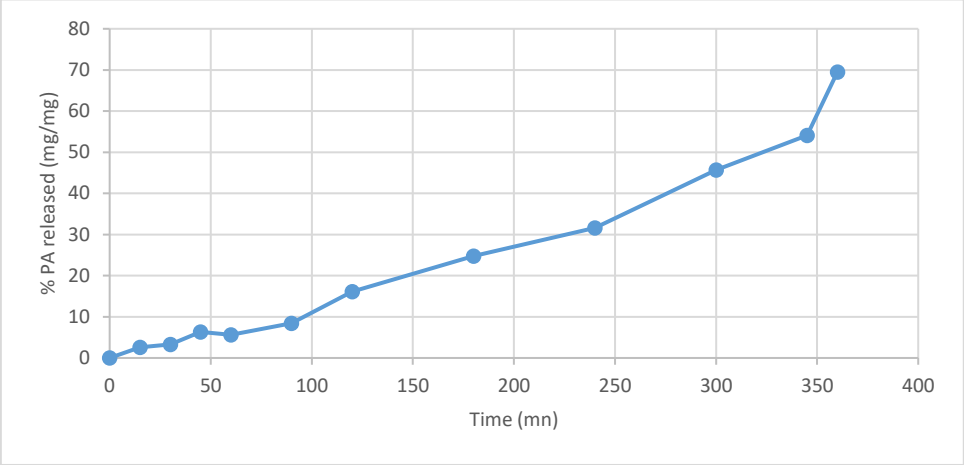

Figure 2: Flavonoid release profile of suppositories containing microparticle

The dissolution curve showed a continuous, sustained release of the active ingredient until the compound was completely dissolved.

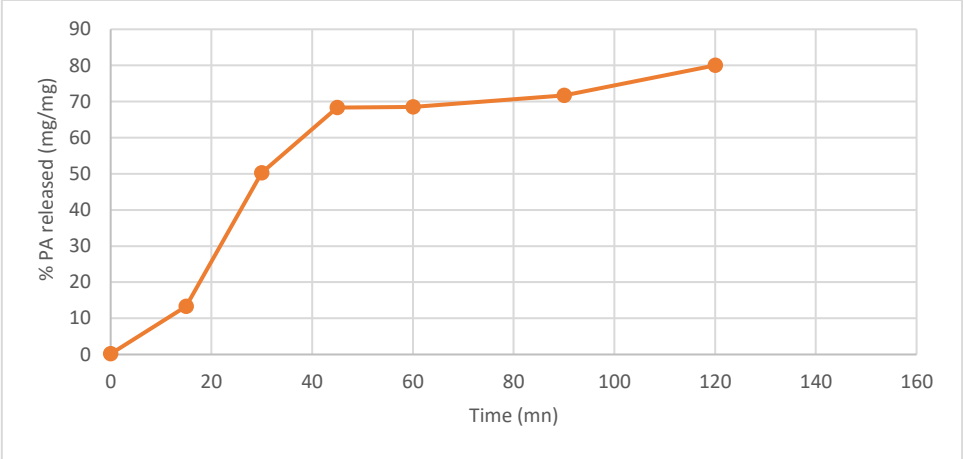

Figure 3: Flavonoid release profile of suppositories containing the extract

The release profile presented showed a rapid release of the active ingredient contained in the suppository, and a shorter release time.

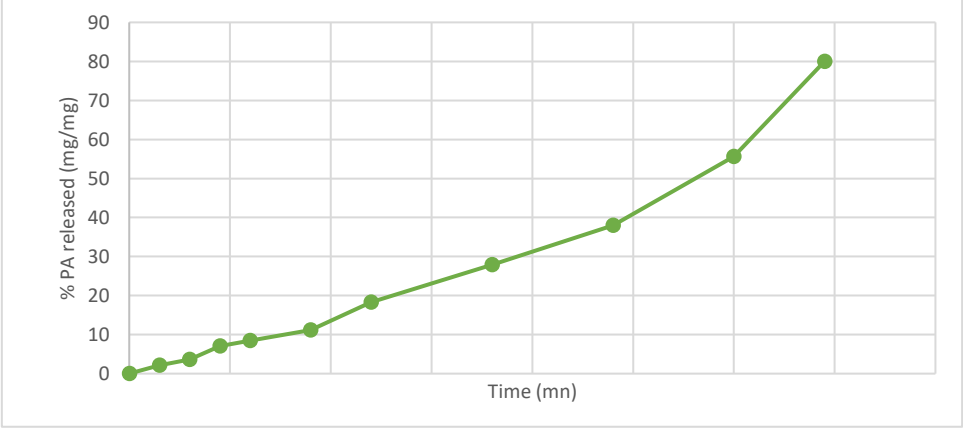

Figure 4: Flavonoid release profile from microparticles

The dissolution profile is broadly similar to that of suppositories containing microparticles.

Comparison of release profile

Dissolution kinetics were studied on suppositories containing microparticles, suppositories containing simple extract and extract-based microparticles.

The percentage of flavonoids released as a function of time is shown in Figure 5.

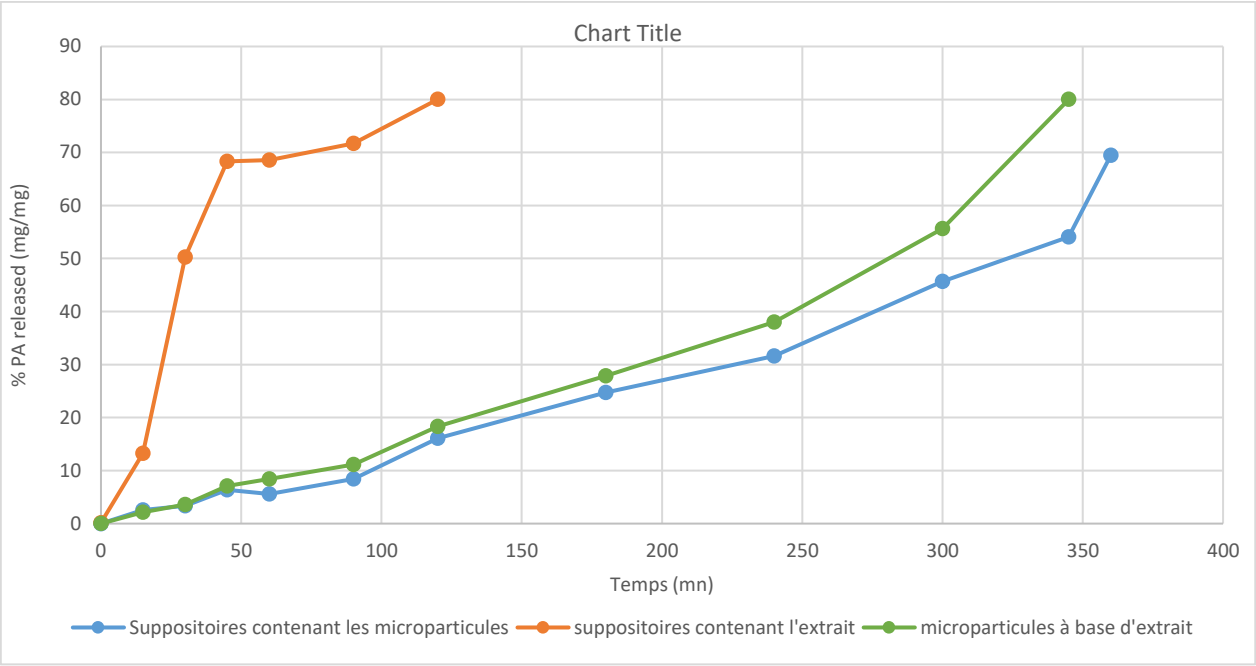

Figure 5: Total flavonoid release profiles for suppositories containing extract and suppositories containing microparticles.

The release rate (VL) expressed as the percentage of flavonoids released as a function of time was 19.85 µg/min for the suppository containing the extract, 6.31µg/min for the suppository containing the microparticles and 7.37 µg/min for the extract-based microparticles.

The release rate of suppositories containing microparticles is lower than that of suppositories containing extract.

DISCUSSION

Landolphia owariensis is an Apocynaceae used in several regions of Black Africa for its various therapeutic virtues, including anti-hemorrhoidal activity. In order to assess the availability of the encapsulated active ingredient, the release kinetics of the flavonoids contained in the suppositories were studied *In vitro* flavonoid release from suppositories containing sodium alginate-based microparticles was assessed by measuring the cumulative percentage release of active ingredient. The dissolution profile of suppositories was determined in phosphate buffer medium at pH=6.8 (KH2PO4) for six (06) hours.

The results obtained showed that flavonoid release from suppositories containing the microparticles exhibited a slower release behavior than that of extract-based microparticles, whose dissolution profile was determined over more than 5 hours.

On the other hand, in vitro flavonoid release from suppositories containing the extract was more rapid. However, the dissolution profile of these suppositories was determined in phosphate buffer medium at pH=6.8 (KH2PO4) for two (02) hours.

Comparison of the *in vitro* dissolution results obtained from the three trials showed that suppositories containing the microparticles behaved differently from those containing the extract. This difference was highlighted, firstly, by the profile of the active ingredient release kinetics of the trials studied and, secondly, by the maximum active ingredient release observed for each trial. The dissolution profile of suppositories containing microparticles was very similar to that of extract-based microparticles. The difference in dissolution time between suppositories containing microparticles and those containing extract would be due to the melting time of the gelatin suppository.

At the end of complete dissolution of each trial, the percentage of active ingredient released for suppositories containing microparticles and those containing extract alone was 69.47% and 80.01% respectively. These results show the influence of several factors on active ingredient release.

The percentage of active ingredient released for suppositories containing extract is the same for extract-based microparticles.

Flavonoids are released sequentially from the microparticles. In fact, release of the PA encapsulated in the polymer matrix takes place in two stages: swelling, characterized by the entry of the dissolving solvent into the matrix, and diffusion of the active ingredient into the solution.

These results suggest that the incorporation of a matrix system in suppositories influences the release profile of encapsulated PA. Similar results were observed in the work of ***Nafti*** **(2008)** and ***Richard and benoit*** **(2000)** [8,11]

In the dissolution test for suppositories containing microparticles and extract-based microparticles, swelling of the microparticles was observed visually. This is probably due to the mucoadhesive natural polymer sodium alginate; a polyelectrolyte that causes maximum swelling. [12,13]

In suppositories containing the extract alone, release was immediate and brief; this would be due to the speed of destruction of the suppository, which would enable the active ingredient to be rapidly made available in the dissolving medium; this would justify the increased dissolution rate of these suppositories.

The rate of suppository destruction is proportional to the solubility and dissolution rate of gelatin in the dissolving medium.

CONCLUSION

The release tests carried out showed the influence of the alginate-based matrix system on AP release kinetics. The release of suppositories containing the microparticles was modified, even slowed down, compared with the rapid release of suppositories containing the extract alone.

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