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Potential analgesic activity of the methanolic F4 fraction of leaf extracts of *Annona senegalensis* Pers. (Annonaceae)

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Abstract

Objectives: Pain management is provided by analgesics. While considerable progress has been made in recent years due to better knowledge of the pathophysiology and mechanism of pain, the search for new, more effective analgesics with fewer side effects remains relevant. Previous work carried out at the pharmacology laboratory of the Faculty of Medicine, Pharmacy and Odontology of UCAD (Senegal) had shown an anti-inflammatory activity of the ether extract, as well as that of the methanolic fraction and of ethyl acetate from *Annona senegalensis* leaves. This study concerns the fractionation of the total methanolic and ethyl acetate fractions by chromatography on a Sephadex column. A phytochemical characterization of the fractions obtained, followed by the study of the analgesic activity of the derivative fractions of the methanolic and ethyl acetate extracts carried out in mice.

Methods: Sephadex gel fractionation yielded ten fractions. Characterization tests were carried out on the total extracts and the different derivatives fractions.

Results: Phytochemical characterization of the fractions revealed the presence of tannins, alkaloids, flavonoids, sterols and triterpenes. The F4 and F'4 fractions, rich in sterols and triterpenes, significantly reduced the number of cramps at low doses (1 mg/kg and 3 mg/kg).

Conclusion: The presence of sterols and triterpenes in the methanolic F4 fraction of the leaves of *Annona senegalensis* could be the cause of the analgesic activity of the plant.

Keywords: *Annona senegalensis*, phytochemistry, sterols and triterpenes, analgesic.

INTRODUCTION¹⁻³

Pain management is provided by analgesics. The treatment of pain is a major public health problem. While considerable progress has been made in recent years due to better knowledge of the pathophysiology and mechanism of pain, in particular thanks to the discovery of endogenous opioids and cannabinoids and the involvement of glia, the search for new analgesics that are more effective and induce fewer side effects remains topical.⁴

Traditional herbal medicines are the recourse of the vast majority of rural populations in developing countries in Africa, where up to 80% of the population use medicinal plants at least once. In Mali, this practice has long been considered a factor in the development of health in the face of numerous pathologies, due to the weakness and high cost of pharmaceutical products. Many strategies to encourage research on these plants have been put in place in recent years and several plants with analgesic activities have been highlighted.⁵

Our study focused on *Annona senegalensis*, commonly called "Mandé Sunsun" in Bambara. It is a shrub 1 to 4 m high, generally found in the open or wooded savannahs of Africa.

The different parts of *Annona senegalensis* (leaves, bark, roots) are used in traditional medicine as an anti-diarrheal, anti-infective, antitussive, healing, decongestant and anti-inflammatory. Previous work carried out in the pharmacology laboratory of the Faculty of Medicine, Pharmacy and Odontology of Dakar, had shown the existence of an anti-inflammatory activity of the total ethereal extract of *Annona senegalensis* leaves. The methanol fraction of the ether extract was more effective in preventing inflammatory edema.⁶

Considering the analgesic action of anti-inflammatory drugs, in this study, we conducted the evaluation of the analgesic action of the methanolic F4 fraction on mouse KOSTER pain study models.⁷

In this study, we will

- Carry out the total extraction of the compounds from the *Annona senegalensis* leaf powder with ether;
- Carry out a liquid-liquid separation of these compounds by using a polar solvent such as methanol;
- Testing the methanolic F4 fraction on the KOSTER pain study model in mice.

MATERIELS AND METHODS

1. Plant material: The plant material consists of leaves of *Annona senegalensis*, the identification of which was carried out at the Pharmacognosy Laboratory of the Faculty of Medicine, Pharmacy and Odontostomatology of

the Cheikh Anta DIOP University of Dakar. Fresh leaves were dried and pulverized.

2. Animal material: The experiments were carried out on mice of an outbred strain selected from the CF1 line (Carworth Farms Strain 1) with an average weight of 25 g.

3. Methods

- Preparation of the extract

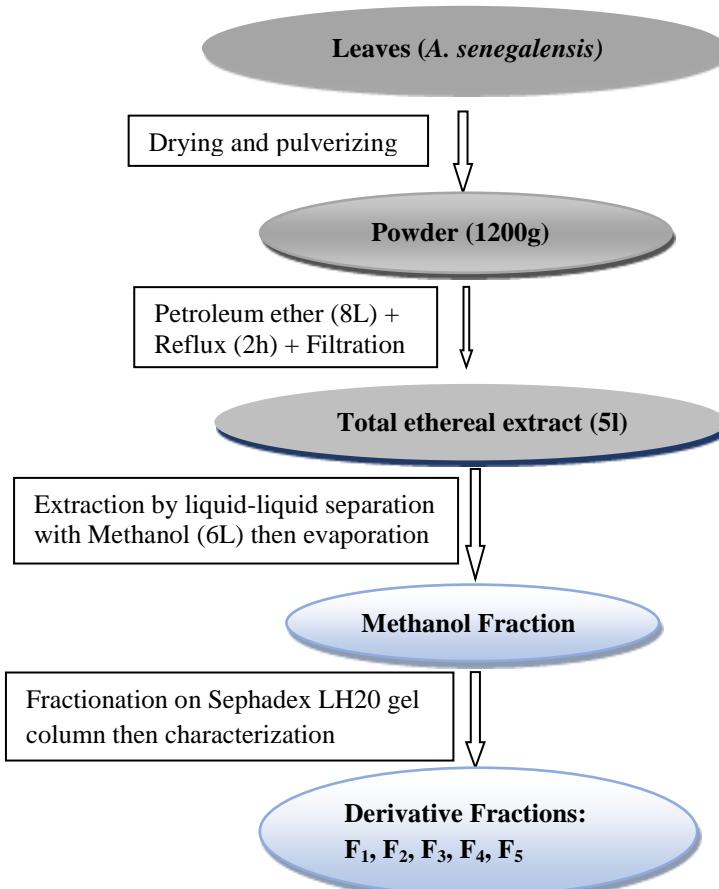


Figure 1: *Annona senegalensis* leaf extraction and fractioning protocol.

- Assessment of analgesic activity

The mice are divided into groups of five, which are then fasted 14 hours before the experiment. The product to be tested, the reference drug or distilled water (0.025 mL/g of mouse), is administered orally 1 hour before the intraperitoneal injection of the acetic acid solution at a dose of 10 mL/kg of mouse. The number of twists performed by each mouse during the 20 min following the administration of the stimulus is counted (see Table 2).

For each group of mice treated, the mean and the standard deviation (SD) are calculated. This average compared to that of the control group made it possible to calculate the percentage of inhibition according to the following formula:

$$\% \text{ Inhibition} = \frac{M_{\text{control}} - M_{\text{trated}}}{M_{\text{control}}} \times 100 \quad M =$$

Mean of the number of twists

RESULTS

Phytochemical profile of *Annona senegalensis* leaves

Phytochemically, the present study revealed the presence of sterols and triterpenes in the total methanolic and ethyl

acetate fractions as well as in the methanolic F4 derivative fractions. The flavonoids are present in all the total fractions but only in the methanolic derivative fraction F5. On the other hand, we note the absence of flavonoids in the methanolic derivative fractions except in the F5 fraction. On the other hand, only the derivative fractions F'3 and F4 methanol revealed the presence of tannins.

Table 1: Results of the specific characterization of tannins, alkaloids, flavonoids and sterols and triterpenes in the different methanolic fractions.

Metabolite	Methanolic extracts				
	Total fraction	Derivative fractions			
		F1	F2	F3	F4
Tannins	+	-	-	+	+
Alkaloids	-	-	-	-	+
Flavonoids	+	-	-	-	+
Sterols and triterpenes	+	-	-	-	+

Note: (+) Presence, (-) Absence.

Table 2: Results of analgesic activity of *Annona senegalensis* leaf extracts

LOTS	Mean of twist ± RSD	Percentage of inhibition (%)
Physiological water (10ml/kg per os)	43,6 ± 2,85	-
Fraction F4 (1mg/kg per os)	28,4 ± 3,79	34,86
Fraction F4 (3mg/kg per os)	16,8 ± 0,59	61,46
AAS (100 mg/kg per os)	17 ± 4	61

DISCUSSIONS

Phytochemically, the present study revealed the presence of sterols and triterpenes in the total methanolic fractions as well as in the methanolic derivative F4 fraction. This probably suggests that the latter would be involved in the prevention of inflammatory edema of the derivative fractions of the total methanolic fractions obtained by previous studies.⁸

These same fractions (total methanolic fractions as well as in the derivative methanolic F4 fraction) revealed the presence of tannins.

Previous work has shown the existence of an anti-inflammatory activity of the methanolic F4 fraction. This fraction was more effective in preventing inflammatory edema.^{6,9}

Considering the analgesic action of anti-inflammatory drugs, in this study we evaluated the analgesic action of the methanolic fraction on pain study models in mice. With regard to the results of the evaluation of the analgesic activity, we found that the control mice developed a large number of cramps (43.6 ± 2.85 cramps for 20 minutes) and gradually after administration of the acetic acid. This is noticed at the beginning by a stretching of the hind legs and a contraction of the intercostal muscles preceding the appearance of frank cramps. Mice treated with acetylsalicylic acid developed reduced number of cramps compared to the control group but similar to animals treated with our product at dose of 3 mg/kg. This is confirmed by the percentages of inhibition observed (61% for ASA against 61.46%). On the other hand, this percentage of inhibition is higher than that of the F4 fraction at 1mg/kg (34.86%). This supports the idea that anti-inflammatory drugs possess analgesic activity. This percentage is higher than that obtained by Sène *et al* who found 37.80 ± 9.00 at 10 mg/kg.⁶

CONCLUSION

The phytochemical characterization of the different fractions revealed the presence of sterols and triterpenes in the total methanolic fraction as well as in the derivative fraction F4. The methanolic F4 fraction at dose of 3 mg/kg showed the

greatest reduction in writhing, 61.46% compared to the standard drug (acetylsalicylic acid) which may suggest that it possesses similar efficacy to aspirin used as an analgesic.

The precise mechanisms involved in the production of the plant's analgesic activity may be caused by the presence of sterols and triterpenes in the methanolic F4 fraction in the leaves.

In perspective, the continuation of this work should be aimed at the isolation of sterols, triterpenes from the F4 fraction and the demonstration of the analgesic activity of the compounds isolated on various pain study models.

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CONFLICTS OF INTEREST: None

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