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# Formulation of an anthelmintic syrup based on the seeds of *Carica papaya* (Caricaceae)

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## Abstract

In traditional medicine, of *Carica papaya* (Caricacea) seeds are used as a coarse powder, in maceration or as an aqueous decoction, for the management of helminthiasis. With the aim of contributing to the management of helminthiasis, this study set out to develop a syrup with anthelmintic properties based on *Carica papaya* L. seeds

The aqueous fluid extract was prepared and subjected to phytochemical screening. A syrup based on this fluid extract was prepared and subjected to a physicochemical and microbiological stability control. To assess the effectiveness of the syrup, a pilot study was initiated. The stools of 441 children aged between 5 and 15 years were examined using Kato-katz technique.

The secondary metabolites present in the fluid extract were polyphenols (1.2 g EAT/ml), alkaloids, catechic tannins, flavonoids and mucilages. The syrup prepared contained 15.15% of fluid extract and responded favorably to the pharmacotechnical and microbiological tests of the European Pharmacopoeia 9th edition.

Only 43 children tested positive for helminth eggs. The syrup based on *Carica papaya* L fluid seeds extract proved to be comparable to Albendazole on *Ascaris lumbricoides* (97.46% reduction rate) and on *Trichuris trichiura* (100% reduction rate) after two administrations of 20 ml 14 days apart. The treatment was also effective against *Necator americanus* and Tenia sp; but the number of cases of these last two parasitoses was too low to allow any reliable conclusion.

Ultimately, the 15.15% syrup of aqueous fluid extract of *Carica papaya* L. seeds proved a reliable solution for the management of *Ascaris lumbricoides* and *Trichuris trichiura* helminthiasis.

**Keywords:** Formulation*; Carica papaya* L.; Syrup; Anthelmintic; Ascaris lumbricoides; *Trichuris trichiura*; Necator americanus; Ténia sp.

## 1. Introduction

Much progress have been made in the prevention and control of helminths through chemotherapy; but the difficulty of accessibility and the cost of drugs limit their use, especially in developing countries and in Cameroon in particular, where low make it impossible to benefit from scientific progress. Medicinal plants are a valuable alternative for the vast majority of rural populations in Africa, where more than 80% of people rely on plants for primary health care [1].

*Carica papaya* L. commonly known as papaya is a small palm-like tree in the Caricaceae family. Widely used in traditional medicine, the dry seeds of its ripe fruits are exploited for their detoxifying, anti-inflammatory, devorming [2,3],

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hypolipidemic and hypoglycemic [4] properties. In addition, several studies like that of Hounzangbe-Adote et *al* have shown the antiparasitic activity of papaya seeds on gastrointestinal strongyles [5]; that of Mpoame *et* al. in 2008 showed the effectiveness of ethanolic extracts of papaya seeds in the treatment of *Ascaris ascariasis* Galli [6].

On this basis the aim of the present study was to formulate a syrup based on *Carica papaya* L. seeds and to evaluate its anthelmintic properties.

## 2. Material and methods

### 2.1. Plant material

The plant material consisted of the seeds of ripe fruits of *Carica papaya* L. (Caricaceae). These fruits from the city of Bafia in the Center region of Cameroon, were purchased in the city of Bangangté (West Cameroon).

### 2.2. Laboratory equipment and reagents

Among other things, we used: a water bath, Dragendorff's reagent, Burchard's reagent, scales, sucrose, sodium benzoate, culture media, petri dishes, an incubator, a microscope, Kato-katz solution.

### 2.3. Preparation of herbal drug

Immediately after purchase, each papaya was washed and split; then the seeds were scooped out with a spoon. Immature seeds and fibers from the fruit flesh of the fruit were removed. The mature seeds were then dried at 60˚C in an oven for 24 hours and passed through a Panasonic model MX-GX1021 electric grinder.

The organoleptic characters and the water content of the powder were recorded; for physicochemical characteristics the color, the odor and the flavor were noted [7]; for water content, a test sample of 0.5 g of powder was introduced into a cleaned, dried and tared watch glass. After 3 hours at 105° C., the container was cooled in a desiccator and then weighed [8]. The water content (T) was calculated the formula:

$$T = \frac{M-(Ms-Mb)}{M} \times 100$$

where : Mb: vacuum glass mass

Ms: mass of the glass containing the powder after drying
M: initial powder mass

The test was carried out three times and the average value was retained

### 2.4. Preparation of the fluid extract

Fluid extracts are liquid preparations of which 1 part by mass or volume corresponds to 1 part by mass of herbal drug. For the percolation procedure, a mass of powder (P) was moistened with twice its mass of water in a percolator and then left to stand. After 24 hours, an amount p /2 g of water was added. The aqueous extract was recovered over time. It took about 8 hours to obtain p grams of fluid extract. The organoleptic characteristics (color, odor and flavor) were recorded. Standard characterization reagents were then used to search for the classic chemical groups: alkaloids, polyphenols, flavonoids, saponins, tannins, coumarins and mucilages [9].

The determination of polyphenols was based on the reduction in an alkaline medium of the phosphotungstic and phosphomolybdic mixture of the Folin-Ciocalteu reagent by the reducing groups of the phenolic compounds, leading to the formation of blue-colored reduction products; the latter exhibit an absorption maximum at 760 nm and the intensity is proportional to the quantity of polyphenols present in the sample. The sample solution and the standard range were prepared in the same way and under the same conditions. The standard phenolic compound used was tannic acid. The total polyphenols content was determined using the equation of the tannic acid calibration curve obtained from a series of five dilutions of the stock solution at 0.125 g/l as shown Table I. This range was carried out three times; the calibration curve was obtained by averaging the using the optical densities for each concentration.

**Table 1** Calibration range for tannic acid

| **Tubes** | **1** | **2** | **3** | **4** | **5** | **6** |
|---|---|---|---|---|---|---|
| Tannic Acid Solution At 0,125g / L (Ml) | 0 | 1 | 2 | 3 | 4 | 5 |
| Distilled Water (Ml) | 5 | 4 | 3 | 2 | 1 | 0 |
| Concentration In G / L | 0 | 0,025 | 0,05 | 0,075 | 0,1 | 0,125 |
| Withdraw 100 Ml Of Each Dilution | | | | | | |
| Folin-Ciocalteu Reagent (Ml) | 500 | 500 | 500 | 500 | 500 | 500 |
| Incubation For 2 Min | | | | | | |
| 20 % $Na_2co_3$ Solution (Ml) | 2 | 2 | 2 | 2 | 2 | 2 |

After 30 minutes in the dark and at 25° ± 1° C, the reading was taken at 760 nm against a blank. Then the calibration line was then plotted to deduce the content of phenolic compounds in the extract and in the galenic preparation. The results were expressed in grams of tannic acid equivalent per ml of syrup.

### 2.5. Syrup formulation and preparation

*2.5.1. Determination of the dose to be administered:*

The work of Okeniyi et al in 2007 [10] indicated that to obtain the anthelmintic effect, 4 g of powdered dry seeds of *Carica papaya* L. must be mixed with 20 ml of honey. According to the definition of the fluid extract, 4g of seed powder corresponds to 4g of fluid extract. The daily dose of syrup therefore consisted the of mixing 4 g of fluid extract with 20 ml of simple syrup with a density of 1.32 (i.e. 26.4 g of simple syrup). The final syrup should therefore have a fluid extract content of 4 / 26.4 x 100 = 15.15%

*2.5.2. Composition and preparation of the syrup:*

Four formulas (F1, F2, F3, F4) with a content of 15.15% of fluid extract of seeds of *Carica papaya* L (table 2) were prepared.

**Table 2** Formulas tested for 100 g of medicated syrup**.**

| | **Formule 1** | **Formule 2** | **Formule 3** | **Formule 4** |
|---|---|---|---|---|
| Fluide extract (g) | 15.15 | 15.15 | 15.15 | 15.15 |
| Simple syrup (g) | 84.85 | 84.85 | 84.85 | 84.85 |
| Sodium benzoate (g) | 0 | 0.1 (= 0,1 %) | 0.3 (= 0,3 %) | 0.5 (= 0,5 %) |

The fluid extract and the preservative were incorporated slowly into the hot simple syrup with slow stirring to homogenize the mixture. After cooling, the mixture was packaged in 60 ml bottles. The preparation ended with quality control.

*2.5.3. Physico-chemical and bacteriological controls*

The syrups were checked every fortnight from the date of manufacture until the 45th day. The following were thus determined:

- the organoleptic characteristics of the preparation: appearance, colour, smell and flavour.
- clarity in daylight.
- the pH using a pH meter
- the density using a densimeter.

chemical stability: The chemical stability test of the medicinal preparation consisted in determining the polyphenol content as a function of time (Day 0, day 15, day 30 and day 45) and expressing it in tannic acid equivalent from the calibration curve.

microbiological control [11]: Three test samples of 1ml of syrup were placed into three sterile jars with 10ml of peptone buffer solution with sodium chloride pH 7.0. A range of four successive 1:10 dilutions of each stock solution was then prepared.

Enumeration of total aerobic germs and of molds and yeasts: For each of the dilutions, the inoculations were made in duplicate in two petri dishes for each culture medium. In a 9 cm Petri dish in 15 to 20 ml of PCA liquefied agar medium (suitable for the culture of bacteria) and a Sabouraud –type liquefied agar medium (suitable for the culture of molds and yeasts) were introduced; after solidification of the media, 0.1 ml of the prepared sample was introduced; The boxes were then incubated for 5 to 7 days at temperatures close to 45˚C, checking whether the enumeration could be carried out. For each test portion, two boxes corresponding to two successive dilutions and presenting the highest number of colonies below 250 for the count of total aerobic germs (ETAG) and 50 for the count of total molds and yeasts (FMLT) were selected. . Then, the bacterial or fungal concentration (N) was calculated as the number of colony forming units per milliliter (CFU/ml) of syrup using the following formula:

$$N = \frac{\Sigma C}{V \times (n1 + 0.1n2) \times d}$$

With :

- N : bacterial or fungal concentration in CFU per ml of syrup
- ΣC: sum of the colonies counted on the two dishes selected
- V: volume of the inoculum (0.1ml on the surface)
- n1: number of dishes retained at the first dilution
- n2: number of dishes retained at the second dilution
- d: Dilution corresponding to the first dish selected, with he least diluted inoculum (dilution factor)

To check the absence of Escherichia coli: 10 ml of trypticase soy liquid medium was mixed with 1 ml of sample, then homogenized and incubated at 37°C for 24 hours. Then, the tube was shaken, and the inoculations were carried out on Mac Conkey agar medium and incubated at 35-37° C. for 48 h after which the colonies were sought.

To check for the absence of Salmonella: 10 ml of trypticase soy liquid medium was mixed with 1 ml of sample, then homogenized and incubated at 37°C for 24 hours. Then, 1ml of enriched culture was taken and inoculated into 10ml of Mueller Kauffmann medium, then incubated at 37°C for 24 h. The subcultures were carried out on Hektoen agar medium and incubated at 37° C. for 48 h after which the colonies were sought.

### 2.6. Determination of anthelmintic activity

The search for anthelmintic activity was carried out on children recruited from some elementary schools in the Ndé division .

#### *2.6.1. Ethical and administrative considerations.*

This study required ethical clearance from the Institutional Ethics Committee of "Université des Montagnes", authorization from the chief physician of the Bangangté health district, authorization from the Ndé departmental delegate for basic education, authorization from the Ndé basic education inspector and research authorization from " Cliniques Universitaires des Montagnes"

The purpose of the study was explained to children, parents and school principals by means of information leaflet before the recording of free consent.

#### *2.6.2. Study population:*

School selection criteria: Any establishment that has not participated in systematic deworming for at least 5 months and whose director and staff were cooperative

Inclusion criteria for children: Children over 5 years who had not taken an anthelmintic in the past six months at the time of stool collection and not having serious pathology. Children whose informed consent form was signed by the parents.

Exclusion criteria: Children whose informed consent was withdrawn during the study or unable to give stools at the time of collection, then children absent at the time of stool collection or treatment administration.

*2.6.3. Treatment administration and follow - up*

A coprological analysis using the Kato-Katz technique cited by Gabrielli [12] preceded the administration of the product. On the day of collection, each child received a sterile stool pot for a stool sample. The collected samples were quickly brought back to the laboratory. The coprological analysis consisted of spreading 20 mg of stool sieve on a microscope slide using a calibrator. A cellophane membrane soaked in Kato's solution was placed over the saddle. After the homogeneous spreading between the slide and the membrane, the reading was made under the microscope and the number of eggs of each species was properly recorded. The results were expressed as eggs per gram (epg) of stool. Those positive for helminth eggs were retained for further study. The information on each child and the result of the analysis were recorded on a technical sheet.

To the subjects in whom the coprological analysis was positive, the administration of the treatment was done randomly. The children were divided into two groups: one receiving *Carica papaya* seed syrup and the other Albendazole suspension (TACIZOL*). Each child received 20 ml of the product on day D0 and 20 ml on day D14. The follow-up examination of the parasite load (post-treatment coprological analysis) was carried out on the seventh day (D7) and then on the twenty-eighth day (D28).

*2.6.4. Treatment evaluation*

The most suitable parasitological indicator for evaluating the efficacy of anthelmintics is the egg reduction rate [13]. For each helminth studied, the egg reduction rate was calculated according to the following formula:

$$\text{Rate of eggs Reduction} = 100 \text{ x} \left(1 - \frac{\text{arithmetic mean of number of eggs during follow-up}}{\text{arithmetic mean of initial number of eggs}}\right)$$

The efficacy of the two drugs studied was evaluated and compared according to the egg reduction rate observed for each parasite species.

## 3. Results

The papaya sample was identified at the National Herbarium of Cameroon at number 18647HNC, yellow variety of Mbam.

### 3.1. Physicochemical characteristics of the extract

**Organoleptic characteristics**: the powder and the aqueous fluid extract of the seeds of *Carica papaya* L. presented the same organoleptic characteristics: dark brown color, cocoa smell, peppery flavor. The water content of the powder was 5.6% ± 2.3%

The results of the phytochemical screening are shown in Table 3.

The phytochemical screening of the fluid extract revealed a significant presence of mucilages. Polyphenols, alkaloids, catechic tannins and flavonoids were also recorded. Saponosides, gallic tannins and coumarins were absent.

The polyphenol assay protocol was carried out three times under the same conditions. For each dilution, the average optical density and the standard deviations were determined, as illustrated in Table 4.

**Table 3** Phytochemical screening of the fluid extract of the seed powder of *Carica papaya* L.

| Tests performed | Reagents | Results |
|---|---|---|
| Polyphenols | 10% Ferric Chloride | ++ |
| Cathetical tanins | Stiasny | + |
| Gallic tanins | 2% Ferric Chloride | - |
| Coumarins | 10% NaOH | - |
| Flavonoids | Shinoda | + |
| Alkaloids | Mayer | + |
| | Dragendorf | ++ |
| Saponosides | Foam index | +++ |

**(+)** = weak presence, (**++**) = medium presence, (**+++**) = strong presence, ( -) = absence

**Table 4** Absorption of tannic acid solutions at 760 nm

| Concentration (g / L) | Average O.D | Standard deviation | Variation Coefficient (%) |
|---|---|---|---|
| **0,025** | 0,0813 | 0,0023 | 2,8 |
| **0,05** | 0,1706 | 0,0040 | 2,3 |
| **0,075** | 0,2533 | 0,0065 | 2,6 |
| **0,1** | 0,3286 | 0,0041 | 1,2 |
| **0,125** | 0,4056 | 0,0011 | 0,3 |
| **Average** | | | 1,9 |

The coefficient of variation was 1.9%. The tannic acid calibration line was obtained as a function of its concentrations between 0.025 and 0.125 g/l and the corresponding mean optical density.

The tannic acid calibration line (figure 1) was used to determine the concentration of polyphenols in the fluid extract of *Carica papaya* seeds It showed that 1ml of fluid extract corresponds to a concentration of 1.2 ± 0.001g tannic acid equivalent of total polyphenols.

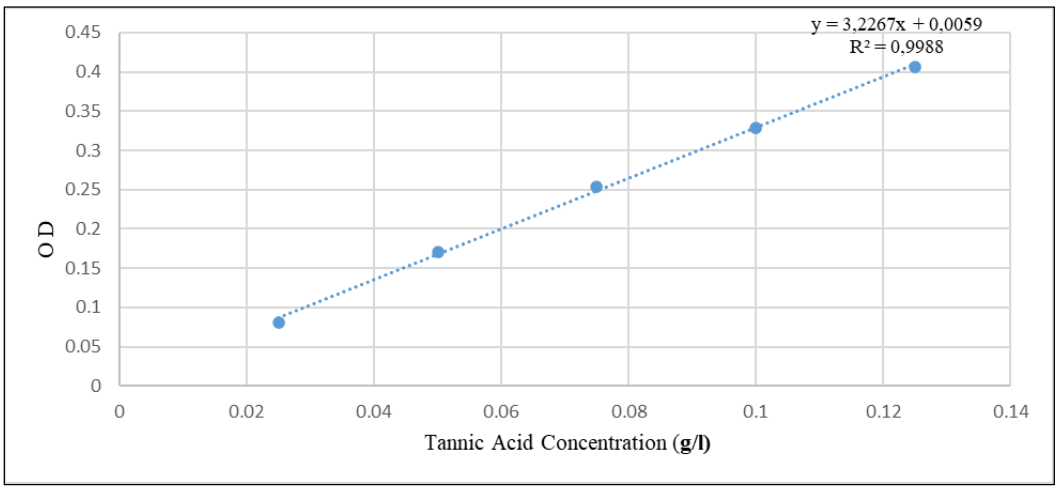


**Figure 1** Tannic acid calibration line

### 3.2. The syrup

*3.2.1. Pharmacotechnical quality*

The syrups obtained were packaged in 60 ml bottles and examined over time. The results of the control of the syrups are presented in Table 5.

**Table 5** Characteristics of formulated syrups

| Days | Syrup Formulas | Colors | Odor | Taste | Appearance | Clarity | Density | pH |
|---|---|---|---|---|---|---|---|---|
| D0 | F1 | Brown | Cocoa | Sweet | Viscous | Clear | 1,28 | 6,12 |
| | F2 | Brown | Cocoa | Sweet | Viscous | Clear | 1,28 | 6,14 |
| | F3 | Brown | Cocoa | Sweet | Viscous | Clear | 1,28 | 6,20 |
| | F4 | Brown | Cocoa | Sweet | Viscous | Clear | 1,27 | 6,23 |
| D30 | F1 | Brown | Cocoa | Sweet | Viscous | Clear | 1,28 | 6,34 |
| | F2 | Brown | Cocoa | Sweet | Viscous | Clear | 1,28 | 6,28 |
| | F3 | Brown | Cocoa | Sweet | Viscous | Clear | 1,28 | 6,23 |
| | F4 | Brown | Cocoa | Sweet | Viscous | Clear | 1,27 | 6,33 |
| D45 | F1 | Brown | Slightly perceptible odor | Sweet | More or Less Viscous | Cloudy | 1,26 | 6,30 |
| | F2 | Brown | Cocoa | Sweet | More or Less Viscous | Clear | 1,28 | 6,29 |
| | F3 | Brown | COcoa | Sweet | Viscous | Clear | 1,28 | 6,25 |
| | F4 | Brown | Cocoa | Sweet | Viscous | Clear | 1,28 | 6,31 |

During storage, the organoleptic characteristics of the syrups did not change for any of the four formulas. The viscosity of F1 and F2 decreased at day 45. On the other hand, it was not modified for the other formulas. The density of the syrups varied slightly between 1.26 and 1.28. The pH of the four formulas fluctuated around 6 during storage. On the 45th day, a deposit of particles was observed in some F1 bottles.

*3.2.2. Microbiological quality*

The results of the microbiological quality of the syrup formulas tested are recorded in Table 6.

**Table 6** Microbiological load of syrups

| Days | Formula | ETAG (UFC/ml) | ETMY (UFC/ml) | Salmonella | *E. coli* |
|---|---|---|---|---|---|
| **Day0** | F1 | 349 ± 129 | 30 ± 12 | Absence | Absence |
| | F2 | 288 ± 37 | 30 ± 12 | | |
| | F3 | 197 ± 80 | 30 ± 12 | | |
| | F4 | 68 ± 60 | 7 ±13 | | |
| **Day15** | F1 | 8128 ± 2208 | 60 ± 26 | Absence | Absence |
| | F2 | 333 ± 146 | 45 ± 23 | | |
| | F3 | 227 ± 159 | 30 ± 34 | | |
| | F4 | 45 ± 45 | 0 | | |
| **Day30** | F1 | 12909 ± 3032 | 370 ± 79 | | |

| | | | | | |
|---|---|---|---|---|---|
| | F2 | 697 ±193 | 60 ±13 | Absence | Absence |
| | F3 | 363 ± 318 | 23 ± 0 | | |
| | F4 | 38 ± 26 | 0 | | |

ETAG = Enumeration of Total Aerobic Germs; ETMY = Enumeration of Total Molds and Yeasts

The different formulas showed a decrease in the bacterial and fungal load as a function of the preservative concentration. On days 15 and 30, the bacterial (ETAG) and fungal (ETMY) load increased significantly in the preservative-free formula (F1). However, these loads remained more or less constant in F2, F3 and F4 where they were particularly very low. The fungal load became negative in F4 from the fifteenth day onwards. *Escherichia Coli* and *Salmonnella* were absent in all preparations

*3.2.3. Chemical stability*

The stability of the preparation was monitored by the content of total polyphenols expressed in tannic acid equivalents. The results obtained are shown in Table 7.

**Table 7** Polyphenol content as a function of time

| Time | Concentration (g EAT / ml of syrup) | Percentage variation (%) |
|---|---|---|
| **Day 0** | 0,281 ± 0,0010 | 0 |
| **Day 15** | 0,278 ± 0,021 | 1 |
| **Day 30** | 0,278 ± 0,021 | 1 |
| **Day 45** | 0,278 ± 0,006 | 1 |

The concentration of total polyphenols measured on day D0 was 0.281 ± 0.001 g TAE / ml of syrup. This content remained virtually unchanged over the 45-day shelf-life.

In view of the results of the previous tests, the formula F4 was chosen; it remained clear and stable throughout the study. It was produced and packaged in 60 ml bottles as shown in Figure 2.

- The attached label specifies:
- The proposed name: (VERICA syrup*)
- The indication;
- The user manual;
- The date of manufacture.


**Figure 2** Final product presentation

### 3.3. Anthelmintic activity

*3.3.1. Parasitological data*

Prevalence of helminthiasis in the population studied : Table VIII shows that among the 441 children examined, 43 passed helminth eggs (prevalence = 9.8%). Boys were more infested (12.8%) than girls (7.1%). Children aged 5 to 10 were less infested (8.3%) than those aged 11 to 15 (12.9%).

**Table 8** Prevalence of intestinal helminthiasis

| | **Subjects examined** | **Positive subjects** | **Prevalence (%)** |
|---|---|---|---|
| Male | 203 | 26 | 12,8 |
| Female | 238 | 17 | 7,1 |
| Age group [5-10] years | 301 | 25 | 8,3 |
| Age group [11-15] years | 140 | 18 | 12,9 |
| Total | 441 | 43 | 9,8 |

The mean age of infected patients was 10 ± 2 years with a minimum of 5 years and a maximum of 15 years. The most represented age group was [5-10] with 25 children (58%). The male sex was the most represented (60.5%), with a sex ratio of 1.5 as shown in Table IX.

**Table 9** Distribution of infested patients by age and sex

| **Variable** | **Boys n(%)** | **Girls n(%)** | **Total n(%)** |
|---|---|---|---|
| **Age [5-10] (ans)** | 12 (46,2 %) | 13 (76,5 %) | 25 (58 %) |
| **Age [11-15] (ans)** | 14 (54 %) | 4 (24 %) | 18 (42 %) |
| **Total** | 26 (60,5 %) | 17 (39,5 %) | 43 (100 %) |

*3.3.2. Initial parasite load by species*

Four parasitic species were found: Ascaris lumbricoides was the most represented with a prevalence of 90.67% ahead of Trichuris trichiura (23.26%), Necator americanus (6.97%) and Ténia sp (4.65%). Among the 43 children, 76.7% were infected with a single parasite species and 23.3% were co-infected.

*3.3.3. Patient care and follow-up*

**Table 10** Characteristics of participants on day 0 (D0)

| | **Verica group** | **Tacizol group** | **P.value** |
|---|---|---|---|
| **Age 5-10 (ans)** | 15 | 10 | 0,0981 |
| **Age 11-15(ans)** | 6 | 12 | 0,1320 |
| **Boys** | 13 | 13 | 0,0603 |
| **Girls** | 8 | 9 | 0,0723 |
| **Aol *am. Lumbricoïdes*** | 493 ± 428 | 529 ± 573 | 0,10 |
| **Aol *n. Americanus*** | 500 | 50 | 0,1324 |
| **Aol *tenia sp.*** | 100 | 50 | 0,1233 |
| **Aol *t. Trichiura*** | 92 ± 66 | 175 ± 132 | 0,1043 |

AOL = Average Ovular Load

Treatment groups. Table 10 presents the characteristics of all the participants in the two groups. The distribution was homogeneous: 21 children were subjected to *Carica papaya* seed syrup (Verica*) and 22 were subjected to the suspension of albendazole ( Tacizol*).

*3.3.4. Evolution of the average egg load (AOL) as a function of time and the treatment received:*

Case of *Ascaris lumbricoides*

Figure 3 shows that by day 7, AOL in both groups had reduced by more than half compared to day 0 (p=0.05); 6 of 20 children (30%) in the *Carica papaya* syrup group were negative. Similarly, 2 of 19 (10.5%).children in the Albendazole group were negative

By day 28, AOL in both groups had fallen sharply. 17 out of 20 children (85%) in the ***Carica papaya*** syrup group and 17 of 19 children (89.5%) in the Albendazole group no longer had eggs in their stools.

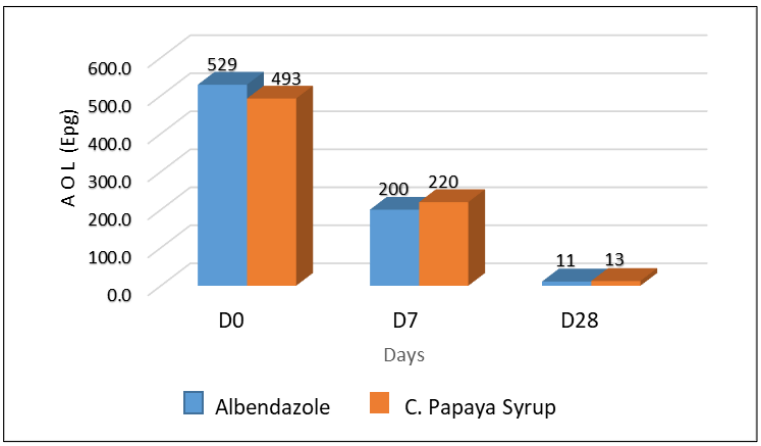


**Figure 3** Evolution of the *Ascaris lumbricoïdes* AOL

Case of *Trichuris trichiura*

Figure 4 shows that by day 7, AOL in both groups had decreased significantly compared to day 0; 1 of 6 children (16.66%) in the Verica syrup* group was tested negative while 2 of 4 children (50%) in the Albendazole group tested negative. By day 28, the AOL in both groups had canceled each other out.

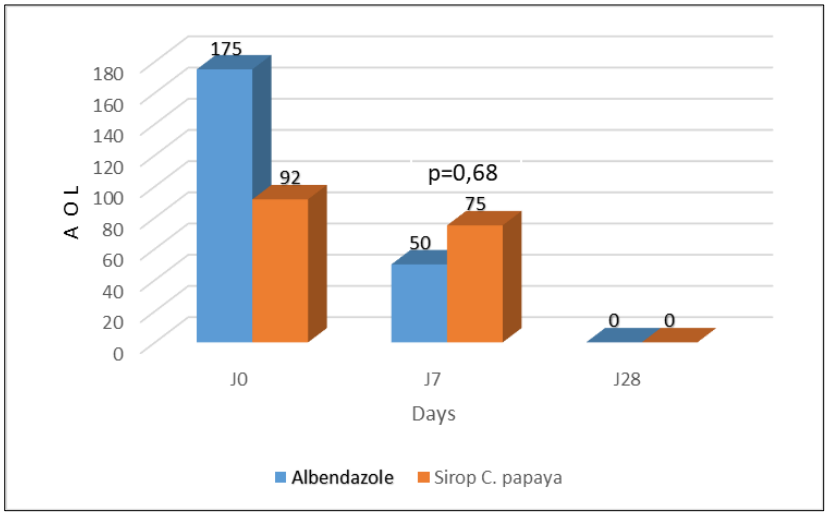


**Figure 4** Evolution of the *Trichuris trichiura* AOL

*3.3.5. Case of Tapeworm sp.*

Figure 5 shows that from the 7th day, all the stools were negative.

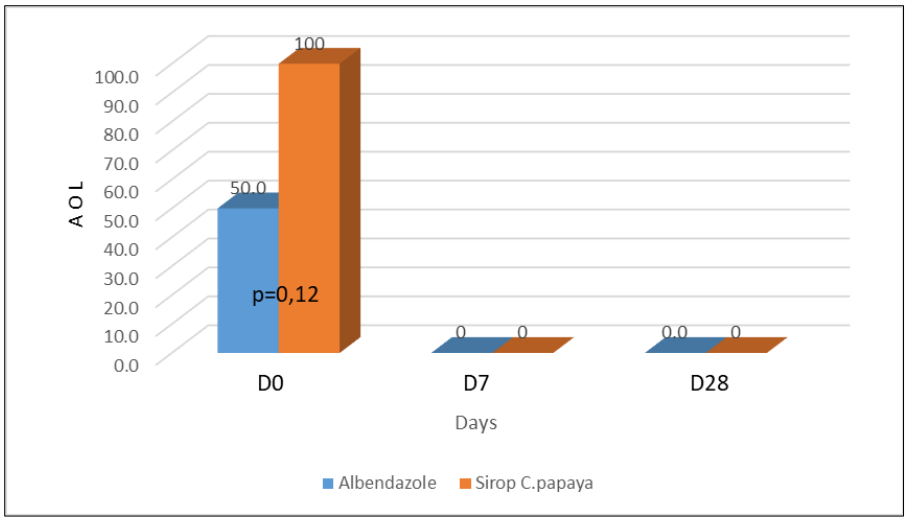


**Figure 5** AOL evolution of Tenia sp.

*3.3.6. Comparative efficacy of the two treatments*

The anthelmintic properties of the syrup based on the fluid extract of the *Carica papaya* L seed fluid extract (VERICA syrup*) and Albendazole (TACIZOL syrup*) are shown in Table 11.

**Table 11 .** Reduction rate (RR) of parasite eggs according to treatment received.

| Treatment | PARASITES | RR AT DAY 7 | RR AT DAY 28 |
|---|---|---|---|
| **Albendazole** | *ascaris lumbricoides* | 62,19 | 97,90 |
| | *necator americanus* | 100 | 100 |
| | *tenia sp* | 100 | 100 |
| | *tenia trichiura* | 71,43 | 100 |
| ***Carica papaya syrup*** | *Ascaris lumbricoides* | 55,33 | 97,46 |
| | *necator americanus* | 100 | 100 |
| | *tenia sp* | 100 | 100 |
| | *trichuris trichiura* | 18,18 | 100 |

Treatment efficacy in both groups at day 28 was comparable. The reduction rate of *Trichuris trichiura*, Tenia sp. and *Necator americanus* was 100%. For *Ascaris lumbricoides* eggs, this rate was 97.9% in the group treated with Albendazole and 97.46% in the group treated with syrup made from seeds of *Carica papaya* L.

## 4. Discussion

The water content of 5.6% attests to the good drying of the drug and guarantees its good conservation. The phytochemical screening revealed several groups of secondary metabolites in the fluid extract of *Carica papaya* L. seeds. The metabolites found (mucilages, polyphenols, alkaloids) are thought to be responsible for the activity as already indicated by Krishna and al in 2008 [14]. The absence of saponosides, gallic tannins and coumarins had already been reported by Lohidas [15] .

Catechic tannins and flavonoids were not significant, while saponins, gallic tannins and coumarins were absent. These results are similar to those obtained by Lohidas et *al* in 2015 [16].

Folin Ciocalteu's method showed that the fluid extract of *Carica papaya* seeds has a titer of 1.2 ± 0.001 g TAE/ml. This method is not specificfor polyphenols; the reaction is crossed with reducing sugars and aromatic amino acids, which can lead to an overestimation of polyphenols, as shown by Kebbab [16].

The sodium benzoate (preservative) concentration of 0.5% was sufficient to control the growth of microorganisms in the syrup; this is in line with the European Pharmacopoeia 9th edition which requires a limit of 104 CFU/ml for ETAG, 102 CFU/ml for ETMY and the absence of E. coli and Salmonella [8].

The overall prevalence of helminthiasis within the 441 children recruited was respectively 8.8% for *Ascaris lumbricoides*, 2.3% for *Trichuris trichiura*, 0.7% for *Necator americanus* and 0.5% for Tenia sp. These results are similar to those of Evi in 2007 in New Caledonia [17].

After the first dose of the drug, the average *Ascaris lumbricoides* egg count fell by more than half in both treatment groups. After the second dose, the reduction in the mean egg count was 97.9% in the Albendazole group and 97.46% in the VERICA (*Carica papaya* L. seed syrup) group (p = 0.0008). In 2007, Okeneyi [10] found an 84% reduction rate in ascariasis treated with *Carica papaya* L seed powder. This suggests that the fluid extract is more effective than the coarse powder.

After the second dose of treatment, the rate of reduction of *Trichuris trichiura* was 100% in both groups. This had already been demonstrated by Okeneyi on the seeds of *Carica papaya* L. [10]. The results obtained thus show comparable efficacy between the Albendazole suspension and the *Carica papaya* L. seed syrup against *Ascaris lumbricoides* and *Trichuris trichiura* parasitosis.

The treatment was also effective against *Necator americanus* and Tenia sp, but the frequency in these two cases was not sufficient to draw a valid conclusion.

## 5. Conclusion

The aim of this study was to develop an anthelmintic syrup based *Carica papaya* L. seeds and to investigate its efficacy on helminths. The syrup obtained contains 15.15% of fluid extract of the plant seeds . Its physicochemical and microbiological stability proved satisfactory.

A pilot study conducted on 43 children aged 5 to 15 showed that the syrup was comparable in efficacy to Albendazole suspension on *Ascaris lumbricoides* and *Trichuris trichiura*, and to a lesser extent on *Necator americanus* and *Tenia* sp. parasitosis.

This syrup could enable *Carica papaya* L seeds to be used rationally for helminthiasis. This pilot trial opens the door to a more elaborate clinical trial that could bring this syrup up to the level of current conventional dewomers.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest.

### *Statement of ethical approval*

This study received approval from the “Universite Des Montagnes” committee.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in this study.

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