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EVALUATION OF HERBAL CREAMS FORMULATED USING ETHANOLIC EXTRACT OF CARICA PAPAYA LEAVES

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ABSTRACT

This research was conducted to evaluate creams formulated using ethanolic extract of *Carica papaya* leaves. The leaves were collected; dried, and extracted by maceration method using ethanol. The antimicrobial activity of extract was determined using the pour plate method for viable counts and the minimum inhibitory concentration (MIC) by agar diffusion method. Test organisms used were *Staphylococcus aureus, Bacilus subtilis, Pseudomonas aeruginosa, Escherichia coli, Aspergillus niger* and *Candida albicans. Carica papaya* leaves ethanolic extract creams were formulated and evaluated for antimicrobial activity and physicochemical properties.

The extract had good antimicrobial activity and MIC of 3.125 mg/ml against all the test organisms except *Aspergillus niger* which was not sensitive even at 100 mg/ml extract concentration. All the formulated creams retained their antibacterial activity but only Formulations F5 to F7 retained their antifungal activity against *Candida albicans.*

The pH of the creams ranged from 4.6 to 7.6, while the viscosity was from 9790 to 95,100 mPas. All the creams were ranked excellent in terms of homogeneity and ease of removal. The spreadability ranged from 2.8±0.00 to 5.35±0.21 cm.

This study showed that creams formulated using ethanolic extract *Carica papaya* leaves have good antimicrobial and physicochemical properties.

Keywords: *Carica papaya*, cream, antimicrobials, bacteria, ethanolic extract

INTRODUCTION

Antimicrobial agents are natural or synthetic substances that kill or inhibit the growth of microbes like as fungi, bacteria and algae **[1, 2]**. Antimicrobials of natural origin are sourced from plants, animals or fungi. Antimicrobials sourced from plants are of great therapeutic importance. They are utilized in the cure of infectious diseases and in mitigating the untoward effects that occur due to use of synthetic antimicrobials **[3, 4]**. The uses of some plants due to their antimicrobial properties have been studied. They include *Pterocarpus santalinoides* **[5, 6]**, *Vernonia ambigua* **[7]**, *Moringa oreifera* **[8]**, *Myrtus communis* and *Flemingia grahamiana* **[9]**.

Creams and ointment that possess antimicrobial properties were formulated by mixing antimicrobial agents and suitable thickening and gelling agents **[10]**. Antimicrobials of plant origin have been formulated into different dosage forms such as creams **[11, 12]**, solutions **[10]**, ointments **[13, 14]** and gels **[15]**. Creams are topical preparations usually applied externally to the skin. They are semi-solid emulsions or viscous liquids. They are formulated as oil-in-water (o/w) or water-in-oil (w/o) creams **[16, 17]**. Pharmaceutical creams contain one or more medicinal agents dissolved or dispersed either in the emulsion or in another type of water -washable base.

Carica papaya also known as pawpaw tree, belong to the family Caricaceae. It is an erect and unbranched tree, which grows very fast up to 7-8 m high. The trunk has diameter of about 20 cm and produces large quantity of latex **[18]**. Several parts of the plant, such as leaves, seeds, fruits, root and their latex are utilized in traditional medicine. Phytochemical studies indicated that cardiac glycosides, saponins and alkaloids are present in the leaves and they are potent free radical scavengers and antimicrobial in action **[19]**. Paw paw is mainly used as antitumor, antibacterial, anti-fungal and wound – healing agent, etc **[2]**. It acts as antibacterial, analgesic, hypotensive,

cardiotonic, amebicide, cholagogue, digestive, emmenagogue, febrifuge, laxative, pectoral, stomachic and vermifuge. It is commonly found in Asia and Nigeria **[20]**.

Previous researchers have shown that different *Carica papaya* extracts demonstrated good activity against some strains of microorganisms **[2, 18, 19, 21]**. This study was conducted to evaluate the antibacterial properties of herbal creams formulated using *Carica papaya* leaves ethanolic extract.

MATERIALS AND METHOD

Materials

The materials used include dried powdered CPLs, absolute ethanol (JHD, China). Emulsifying wax (Lodha Chemicals, India), white soft paraffin (HP Chemical, India), liquid paraffin (Niram Chemicals, India), chlorocresol (Lodha Chemicals, India), nutrient agar (Titan Biotech, India), Sabourand dextrose agar (Life Save Biotec, USA), Mueller Hinton agar (Titan Biotech, India), ketoconazole, gentamicin.

Organisms used:

Staphylococcus aureus, Bacilus subtilis, Pseudomonas aeruginosa, Escherichia coli, Aspergillus niger and *Candida albicans* were obtained from the Department of Pharmaceutical Microbiology, Delta State University, Abraka.

Collection and identification of plant material

The *Carica papaya* leaves were obtained from the Department of Pharmacognosy's botanical garden in Delta State University, Abraka. Dr. Emmanuel Ikpefan of same Department identified it. The leaves were dried under shade at room temperature. The dried leaves were ground to coarse powder.

Preparation of ethanolic extract of *Carica papaya* leaves

A 100 g of the coarse powdered leaves was macerated in 1000 ml of 70% v/v ethanol for 72 hours with agitation at frequent intervals. It was filtered using muslin cloth and the extract obtained was oven dried at 70°C. The concentrated extract was stored in a porcelain dish, carefully wrapped in aluminum foil. The percentage yield was calculated using **equation 1**.

$$\text{Percentage yield} = \frac{\text{weight of extract (g)}}{\text{Weight of powdered leaves (g)}} \text{ X } 100$$

Preparation of Agar and Overnight Broth

A 1.3 g/100 ml quantity of freshly prepared nutrient agar was sterilized for 15 minutes at 121°C and100 kPa using an autoclave (Leader model: GP/50/CLAD/250/HYD). The agar was poured into six sterile bijou bottles under aseptic measures. The bottles were placed in a slanted position on a wooden test tube rack to solidify. On solidification, the organisms, *Staphylococcus*

aureus, *Bacillus subtilis. Escherichia coli*, *Pseudomonas aeruginosa, Candida albicans* and *Aspergillus niger* were inoculated onto the slants respectively and labeled. The slants containing the bacteria were incubated for 24 hours at 37°C using an incubator (Uniscope SM9052 laboratory incubator) and the slant containing the fungi was incubated for 72 hours at 25°C.

Antimicrobial Sensitivity

A 3.8 g/100 ml quantity of Mueller Hinton agar (MHA) and 6.5 g/100 ml of Sabourand Dextrose agar (SDA) were sterilized and poured into twelve Petri dishes (eight containing MHA and four containing SDA) and allowed to solidify. The Petri dishes were inoculated respectively by streaking the surface gently with swab stick; MHA for bacteria and SDA for fungi. Six holes were bored using 6 mm diameter cork-borer. The holes were labelled in order of two fold serial dilution (i.e 100, 50, 25, 12.5, 6.25 and 3.125 mg/ml). A hole was bored in the middle for the negative control (distilled water). The different concentrations of the extracts and negative control were transferred aseptically into the respective holes. The Petri dishes that contained the bacteria were covered with aluminum foil and incubated for 24 hours at 37°C, while the Petri dishes that contained the fungi were wrapped with aluminum foil and incubated for 48 hours at 37°C. After 24 and 48 hours intervals respectively, the different zones of inhibition were determined to the nearest millimeter along the two axes and the mean of two readings were calculated. These operations were repeated using gentamicin (40 mg/ml) as positive control for the bacteria inoculums and ketoconazole (20 mg/ml) for the fungal inoculums.

Determination of the Minimum Inhibitory Concentration (MIC)

Six Petri dishes each were used for the MIC tests for bacteria and fungi respectively. For the bacteria, each Petri dish was divided into four equal parts and labelled appropriately (one quarter for *Pseudomonas aeruginosa, Bacillus subtilis, Escherichia coli* and *Staphylococcus aureus* respectively*)*. For the fungi, each Petri dish was divided into two equal halves (one-half for *Candida albicans*, while the other for *Apergillus niger*. A 7.6 g/200 ml quantity of MHA and 13 g/200 ml of SDA were prepared and sterilized using the autoclave at 121°C and100 kPa for 15 minutes. Two fold dilutions of the extract were prepared (100, 50, 25, 12.5, 6.625 and 3.125 mg/ml respectively). A 1ml quantity of the dilutions of the extracts was instilled into six Petri dishes respectively and then, 19 ml of the Mueller Hinton agar was poured into

each of the six Petri dishes containing the extracts. The plates were rocked gently to ensure that the agar and extract mixed uniformly. They were allowed to solidify. The plates were inoculated with the overnight broth culture of the respective organisms using sterile wire loop. The plates were covered with aluminum foils and incubated for 24 hours at 37°C. The MIC of the extract for the organisms were determined after the 24 hours incubation period. This operation was repeated using SDA and the fungi but they were incubated for 48 hours at 37°C. The MIC is the minimum concentration of the extracts that inhibited the growth of the microorganisms.

Preparation of creams

A 100 g quantity of emulsifying cream base was prepared by weighing and melting thirty grams (30 g) of emulsifying wax in water-bath at 70 ± 0.5°C. A 23.27 ml (20 g) quantity of liquid paraffin and 50 g of white soft paraffin were incorporated into the mixture. It was removed from the water-bath and stirred continuously until it became cold **[22]**.

The *Carica papaya* leaves ethanolic extract creams were prepared using the formula in Table 1. A 30 g quantity of emulsifying cream base was weighed in a porcelain dish and melted in a water bath at 70 ± 0.5°C. The required amount of the ethanolic extract was incorporated into the molten cream base and continuously agitated until it was evenly mixed. Sufficient quantity of warm distilled water was incorporated into the mixture in portions and stirred until a uniform blend was obtained. The cream was allowed to cool before it was poured into the cream jar and labelled properly. Glycerol was added to formulation F6.

Table 1: Composition of the formulated creams

Ingredients	F1	F2	F3	F4	F5	F6	F7
Carica papaya extract (g)	0.3125	0.3125	0.625	0.625	-	0.625	0.625
Emulsifying ointment (g)	30	30	30	30	30	30	45
Chlorocresol (g)	-	0.1	0.1	-	0.1	0.1	01
Glycerol	-	-	-	-	-	0.1	-
Water (g)	69.700	69.600	69.275	69.375	69.900	69.175	54.275
Total (g)	100	100	100	100	100	100	100

Physical evaluation of the creams

Organoleptic test

Organoleptic properties such as the appearance, texture, color of each formulation were determined **[23]**.

Homogeneity

The formulated creams were evaluated for homogeneity by visual inspection **[24]**.

Ease of Removal

This was determined by using a fingertip to scoop little quantity of each of the formulations and these were applied on the

skin. The applied creams were removed with running tap water **[25]**.

Determination of pH

The pH of the formulated creams were determined with a digital pH meter.

Spreadability

The method of Raju et al **[26]** was used with slight modification. A 0.1 g quantity of cream was placed between two glass plates. A weight of 300 g was placed on top of the upper plate for 5 min. The diameter of the circle formed by the cream was measured and recorded as its spreadability.

Determination of Viscosity

The formulated creams' viscosity was evaluated with spindle #4 of a Brookfield viscometer, at different speeds (6, 12, 30 and 60 rpm).

Antimicrobial activity of formulated creams

The zones of inhibition of the formulated creams were determined using the disc diffusion method **[27]**. MHA was prepared and poured into a Petri dish to solidify. The overnight broth of the test organisms were uniformly spread over the surface of the sterile agar plate with a sterile swab stick. SDA was used for the antifungal studies. Paper discs were smeared with the different herbal cream formulations and the control was smeared with either gentamicin for bacteria or ketoconazole for fungi. The plates were incubated at 37°C for 24 and 48 hours respectively. The diameters of the zones of inhibition were measured. Clear zones of inhibition indicated susceptibility of the organisms, while absence of such zones indicated resistance.

Stability studies

Accelerated stability studies were conducted on the formulated creams at 45 ± 0.5°C for one month. The parameters evaluated were the pH, homogeneity and ease of removal of the formulations at different time intervals **[24]**.

RESULTS AND DISCUSSION

The percentage yield of the ethanolic extract of dried *Carica papaya* leaves was 49.84%.

The result in **Table 2** shows that the extract had MIC of 3.125 mg/ml for all the test organisms except *Aspergillus niger* which was resistant even at 100 mg/ml.

The sensitivity patterns indicated that all concentrations of the extract were effective against the selected bacteria strains. They were all effective against *Candida albicans* but ineffective against *Aspergillus niger*. The sensitivity pattern was in agreement with the findings of Mba-Omeje *et al* **[19]** which showed IZD of 16 -22 mm for *S. aureus* and 20-28 mm for *E. coli* when methanolic extract of *Carica papaya* was used.

Subramaniam *et al* **[2]** also reported susceptibility of *S aureus*, *E. coli* and *C. albicans* to methanol extract of *Carica papaya*. Aruljothi *et al* **[28]** reported that the use of acetone leaf extract of *C. papaya* against wound infection-causing org;ppanisms produced noticeable effect on gram negative bacteria especially *Pseudomonas sp*. There was a progressive reduction in the zones of inhibition from higher to lower concentrations for the sensitive test organisms (i.e 100 > 50 > 25 > 12.5 > 6.25 > 3.125 mg/ml). The positive controls, ketoconazole (20 mg/ml) and gentamycin (40 mg/ml) produced higher zones of inhibition than the extract.

Table 3 shows the results obtained when the herbal creams were subjected to physical evaluation tests.

Appearance: All the cream formulations except F5 were cream in colour. Formulation F5 was white in colour and this may due to absence of the extract in it.

Odour: The cream formulations have slight phenolic smell except F1 and F4. The slight phenolic odour may be attributed to the presence of chlorocresol in the formulations.

pH: The creams pH ranged between 4.6 and 7.6. Formulations F1, F5, F6 and F7 were within the normal pH range of the skin. They could be applied on the skin without any irritating effect.

Homogeneity: All the creams had good homogeneity. This showed that the ingredients were uniformly mixed especially while cooling.

Spreadability: Formulations F1, F2, F4, F5 and F6 showed better spreadability when compared to F2 and F7. Spreadability of a cream or gel is its ability to evenly spread on the skin. Its role in the administration of a standard dose of a drug to the skin and the therapeutic effect of the topical therapy is salient **[29]**.

Ease of removal: All the formulations were easily washed off by running water. This showed that the formulated creams are oil-in-water creams **[8]**.

Viscosity: The viscosity of the formulations ranged from 9,790 to 95,100 mPas. The viscosity curves **(Figure 1)** indicate that the formulated creams exhibit pseudoplastic flow. Their viscosities decreased as shear stress was increased.

Antimicrobial sensitivity of the Herbal cream

The antimicrobial susceptibility tests **(Table 4)**, indicated that all the formulated herbal creams produced remarkable zones of inhibitions against all bacteria except F1 that showed no activity against *E.coli*.

Formulations F5, F6 and F7 had activity against both *C. albicans* and *A. niger,* while formulation F4 was active against *C. albicans* but not against *A. niger.* Formulations F1 to F3 had no activity against the fungi. The formulations F3, F4, F6 and F7 that were produced with higher concentration of the extract (0.625 mg/ml) exhibited higher zones of inhibition than F1 and F2, which were formulated with lower extract concentration (0.3125 mg/ml).

Stability: The stability evaluation carried out on the different cream formulations showed that there were no changes in the physical appearance of the formulations, after the 40 days evaluation period.

Table 2: Zones of inhibition and MIC of the *Carica papaya* leaves extract on the test organisms

S/N	Organism	Zones of inhibition (mm) of different extract concentrations						Gentamicin	Ketoconazole
		100 mg/ml	50 mg/ml	25 mg/ml	12.5 mg/ml	6.25 mg/ml	3.125 mg/ml		
1	*S. aureus*	14	11.5	11	10	7	8	34	-
2	*B. substilis*	13	11	8	8	6	4	29	-
3	*E. coli*	10	8	7	7	5	7	34	-
4	*P. aeruginosa*	16	12	11	12	11	8	39	-
5	*C. albicans*	16	14	8	6	5	5	-	20
6	*A. niger*	-	-	-	-	-	-	-	17

Table 3: Physical evaluations of the formulated creams

Formulation	F1	F2	F3	F4	F5	F6	F7
Colour	Cream	Cream	Cream	Cream	White	Cream	Cream
Odour	Odourless	Slightly phenolic	Slightly phenolic	Odourless	Slightly phenolic	Slightly phenolic	Slightly phenolic
Ph	6.5	7.2	7.6	7.6	4.6	5.7	5.0
Spreadability	4.8±0.00	4.2±0.00	2.8±0.00	5.35±0.21	4.5±0.00	4.35±0.21	3.5±0.00
Homogeneity	Good	Good	Good	Good	Good	Good	Good
Ease of removal	Easy	Easy	Easy	Easy	Easy	Easy	Easy

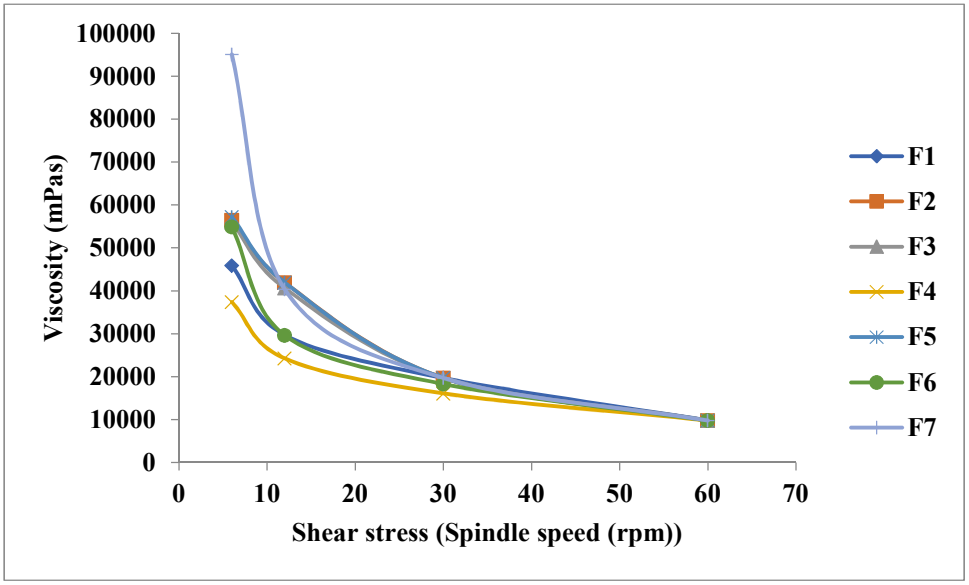

Figure 1: Viscosity curve of *Carica papaya* cream formulations

Table 4: Zones of inhibition of the various formulations of *Carica papaya* cream on the test organisms

S/N	Organism	Formulation Codes/Susceptibility (mm)								
		F1	F2	F3	F4	F5	F6	F7	Gentamicin	Ketoconazole
1	*S. aureus*	2.5	3.5	7	7.5	1	9	11	39	-
2	*B. subtilis*	4	7	9	9.5	4	11	11.5	34	-
3	*E. coli*	-	6	11.5	9	2	10.5	12	30	-
4	*P. aeruginosa*	3	9	12	10	2	12	13	44	-
5	*C. albicans*	-	-	-	3.5	3	5	5.5	-	22
6	*A. niger*	-	-	-	-	2	2	4	-	20

CONCLUSION

This study has shown that *Carica papaya* leaves ethanolic extract has good antibacterial activity against *Staphylococcus aureus, Escherichia coli, Bacillus subtilis* and *Pseudomonas aeruginosa.* It has antifungal activity against *Candida albicans* but no activity against *Aspergillus niger*.

There was no loss of antibacterial activity on formulation of the extract into creams. Formulations F4 to F6 retained the extracts antifungal activity against *C. albicans* unlike formulations F1 to F3.

The organoleptic properties of the formulated creams were within standard ranges, although, the formulated creams were slightly acidic but were within the normal pH range of the skin. The formulated creams were also stable.

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