Journal of Bioscience and Biotechnology Discovery
Volume 6(4), pages 38-45, October 2021
Article Number: 07EDCF682
ISSN: 2536-7064
https://doi.org/10.31248/JBBD2021.157
https://integrityresjournals.org/journal/JBBD
Full Length Research

Development of novel lozenges tablets containing chloroform root extract of *Adenodolichos paniculatus* (hua) Hutch. & Dalz (Fabaceae)

Kyahar, I. F.[1]*, Onwuliri, A. E.[1], Ehinmidu, J. O.[2] and Oladosu, P.O.[3]

[1]Department of Pharmaceutical Microbiology and Biotechnology, University of Jos, Jos, Nigeria.
[2]Department of Pharmaceutics and Pharmaceutical Microbiology, Ahmadu Bello University Zaria, Nigeria.
[3]Department of Microbiology and Biotechnology, National Institute for Pharmaceutical Research and Development, Abuja, Nigeria.

*Corresponding author. Email: kyaharfriday@yahoo.com

Received 1st September, 2021; Accepted 24th September, 2021

ABSTRACT: Medicinal plants have been widely used as a source of medicine to combat ailments including infectious disease and may constitute a reservoir of new antimicrobial substances to be developed. *Adenodolichos paniculatus* is a medicinal plant widely used for the traditional remedy of coughs, dysentery, diarrhea and sore throat infections. The aim of this study was to formulate *Adenodolichos paniculatus* chloroform root extract as a novel lozenge tablet and to evaluate their antibacterial and tablet parameters. *Streptococcus pyogenes*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* were used as the test bacteria. The extract was formulated into Lozenge tablets using wet granulation method with gelatin and sucrose as binder and diluent respectively. Uniformity of weight, hardness, friability, bacterial susceptibility tests were conducted on two batches of formulated Lozenges of 25 and 50 mg and a reference standard formulation, Strepsils^{R}, containing Amylmetacresol (0.6 mg) and 2,4-dichlorobenzyl alcohol (2 mg). Results showed that both batches passed the tablet weight uniformity test with mean crushing strengths of 10.4 and 13.1 KgF, respectively. *S. pyogenes*, *S. aureus* and *P. aeruginosa* were susceptible to both batches with inhibition zones ranging from 18.00-25.50, 16.00-21.50 and 9.00-12.00 mm and 22.00-26.50, 20.50-23.00 and 10.00-13.00 mm respectively. The bacterial susceptibility compared favorably with the standard formulation as the difference between the inhibition zone diameters of each test bacteria and the standard formulation was not statistically significant ($p>0.05$). The result indicated that there was a delayed release of the extract from the test lozenges with batch 1 (25 mg) being from 30 minutes and batch 2 (50 mg) from 60 minutes compared to that of the standard formulation which had immediate drug release at 5 minutes. The method used for the formulation and the sticky nature of the extract might not allow and promote the immediate release of the antibacterial extract from the dosage form.

Keywords: *Adenodolichos paniculatus*, antibacterial activity, chloroform extract, lozenge formulation.

INTRODUCTION

Pathogenic bacteria constitute menace to human health and contribute to microbial infections suffered in the tropics (Esimone et al., 2003). Plants secondary metabolites contribute to the pharmacological activities such as analgesics, antitumor, antibacterial properties making them as sources of lead compounds for development of new drugs (Dar et al, 2017). There is increasing interest in natural antibacterial agents due to problem of resistance crowding the existing antibacterial agents (Olaniyi, 2005).

Adenodolichos paniculatus (Family: Fabaceae) is a

shrub of 4 to 5 m high and found in the savanna, bush and jungle, from Guinea to Northern Nigeria, and across to Sudan. The folkloric uses include dressing of burns, dysentery, liver trouble, venereal diseases, tonsilitis, dysentery, diarrhea, blennorrhoea and also used as a pain-killer (Hutchinson and Dalziel, 1958a).

It is also known by various ethnic names such as *kpàrák* (Berom), *gargung* (Mwaghavul), *kilikainawa* (Fulfulde) and waken *wuta* (Hausa) to mention but a few in Nigeria (Sani et al., 2010). It is one of the important medicinal plants with widespread traditional uses in the remedy and management of sore throat infections in Pushit community in Mangu Local Government Area, Plateau state.

In previous research, it has been reported that the chloroform root extract of *Adenodolichos paniculatus* exhibited significant antibacterial activities against *Streptococcus pyogenes*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* that were comparable to that of a standard antibiotic drug, ofloxacin with MIC of 1.56, 6.25 and 25.00 mg/ml for each test bacteria. The activity of the root extract was linked to five phytochemical constituents which included flavonoids, tannins, terpenoids, saponins and phenols (Kyahar et al., 2021).

Sani et al. (2010) reported that the methanolic leaf extract of *Adenodolichos paniculatus* exhibited significant and dose dependent analgesic and anti-inflammatory effects that were comparable to that of a standard analgesic and anti-inflammatory drug, ketoprofen. These preliminary results, coupled with the folkloric use of the plant in the treatment of sore throat infections and tonsillitis suggest that *Adenodolichos paniculatus* is a good candidate for formulation into lozenges for the possible treatment of mouth and throat infections.

Lozenges are solid, single-dose preparations designed to be sucked to obtain, usually, a local effect in the oral cavity and the throat (Sastry et al., 2000). Lozenges are intended to dissolve slowly (over 5-10 min) in the mouth and so release the drug dissolved in the saliva (Deepika et el., 2014; Nagoba et al., 2011). One of the commonest brands of throat Lozenge found in pharmacy shops in Nigeria is Strepsils^{R}. Its formulation form includes other excipients that promote rapid release of the active ingredients (Swarbrick and Boylan, 2002), while possessing antibacterial. Strepsils^{R} tablet [Amylmetacresol (0.6mg) and 2,4-dichlorobenzyl alcohol (2 mg)] is used in the treatment of infections of the gum, mouth and throat. Because of the high risk of misuse, this Lozenge is suspected to be liable to microbial resistance. Moreover, because it is sweetened, several people sometimes use it as sweet or candy.

Therefore, the aim of this study was to formulate *Adenodolichos paniculatus* chloroform root extract as a novel lozenge tablet and to evaluate their antibacterial and some of their tablet parameters that will be useable and reliable oral dosage form for treatment of sore throat infections caused by any of the test bacteria.

MATERIALS AND METHODS

The roots of the plant *Adenodolichos paniculatus* were the specimen used for this study. The typed and non-typed bacteria used for the study included: *Staphylococcus aureus*-ATCC6538 and *Pseudomonas aeruginosa*-ATCC9027 which were obtained from central diagnostic lab-National Veterinary Research Institute (NVRI), Vom, Plateau State; and *Streptococcus pyogenes*- Clinical isolate was obtained from Department of Microbiology and Bacteriology, National Institute for Pharmaceutical Research and Development-Diagnostic Centre, Abuja-Nigeria.

Collection, identification and extraction of plant materials

The plant *Adenodolichos paniculatus*, was selected based on traditional remedy history. The information about the local and traditional application of the plant was collected during and after sampling through oral interviews with an herbalist in Pushit-Mangu LGA. The plant specimens were harvested from the wild plant between October 2018 and March 2019. An herbalist was consulted as his experience was used to determine the best collection time and accurate location of the plant within the District of Pushit in Mangu LGA of Plateau State. The collected roots were cleaned, cut into bits, spread over a rack covered with cheesecloth and air-dried at room temperature (25-28°C). The dried samples were pulverized with a mechanical grinder, sieved with 2.5 mm sieve and packed into clean, dried bottles and covered tightly. The bottles were labeled with the plant name and date of collection and stored at room temperature (25-28°C) until ready for extraction. The plant was identified as *Adenodolichos paniculatus* on voucher number FHJ 205 and deposited at the Herbarium unit of Federal College of Forestry, Jos. The bioactive constituents of the plant were extracted with five solvent systems (n-hexane, ethyl acetate, chloroform, methanol and water). This was to ensure that compounds with a wide range of polarity could be extracted. The serial maceration extraction technique was employed and successive extraction was carried out with solvents of increasing polarity from non-polar to more polar solvents (Banu and Catherine, 2015).

One kilogram (1 kg) of the powdered sample was extracted in a flat bottom flask with 2.5 liters hexane by maceration for 24 hours with intermittent shaking. The sample mixture was filtered with muslin cloth and with vacuum pump filtration. The filtrate was concentrated using rotary vacuum evaporator at 40˚C. The concentrated/dried extract was collected into a pre-weighed sterile universal bottle and stored until required for microbiological assay. This process was repeated using chloroform, ethyl acetate and methanol. Using Ali et al. (2011) method, the percentage extract yields of the

Table 1. formulation formula lozenge tablet preparation.

Ingredients	Batch 1 (1 x MIC)	Batch 2 (2 x MIC)
A. paniculatus extract	25 mg	50 mg
Sucrose	975 mg	1950 mg
Gelatin	2% w/v	2% w/v
Total weight	1000 mg	2000 mg

plant samples were calculated as:

$$\text{Percentage extract yield (\%)} = \frac{\text{Weight of dried extract}}{\text{Weight of dried powder}} \text{x } 100$$

Preparation of granules and compression

The wet granulation method was employed for the lozenge tablet preparation. The formulation formula was as shown in Table 1. Chloroform root extract weighing 25 and 50 mg each were mixed with 975 and 1950 mg of sucrose for batch 1 and 2 respectively and triturated thoroughly with mortar and pestle into homogeneous mass. The blended was moistened with gelatin aqueous solution for both batches. The wet mass was passed through sieve number 850 micrometer (mm) and the granules were dried in hot air oven at 40°C for 1 hour. The formulations (1000 and 2000 mg) were then compressed in a single punch tableting machine (THP Tablet Press, Shanghai) with compression of 11KN separately (Deepika et al., 2014).

Physicochemical evaluation of *A. paniculatus* lozenges tablets

Weight variation

Weight variation test was done by weighing ten lozenges individually and their average weight was determined. Then individual lozenge weight was compared with average weight (Indian Pharmacopoeia, 2010).

$$\text{Weight Variation} = \frac{\text{Average Weight} - \text{Individual tab weight}}{\text{Average weight}}$$

Hardness test

Ten tablets were subjected to the hardness (tablet crushing) test. Lozenge was placed between the spindle and anvil of the tester and the calibrated length adjusted to zero. The knob was then screwed to apply a diametric compression force on the tablet and the position on the calibrated length at which the tablet broke was recorded in Kg units. The force required to crush/break the tablet was measured in Kg force (Kgf). The mean hardness and standard deviation values was then recorded.

Friability test

The friability test was conducted using Roche Friabilator tester. Ten clean lozenges were weighed (W1) and lozenges were placed in the Friabilator/drum and adjusted the instrument at 100 rotation (i.e 25 rpm for four minutes) and removed the lozenge. The tested lozenges are dusted with a brush and then accurately weighed (W2). The friability was expressed as a weight loss percentage (Indian Pharmacopoeia, 2010). The tablets were weighed together before (Wo) and friabilated. The friabilated tablets was re-weight (W1). Friability was calculated as follow:

$$\text{F} = \frac{\text{W0} - \text{W1}}{\text{W0}} \; x \; 100$$

Where Wo = weight of tablets before the test and W1 = weight of tablets after the test

***In-vitro* drug release studies**

Preparation of normal saline-saliva mixture

Sodium chloride (0.9 g) was dissolved in 95 ml distilled water and volume was made up to 100 ml with human saliva. This preparation made a provision for isotonicity of actual human saliva, as well as necessary presence of resident salivary enzymes which may impact on lozenge activity in normal clinical use condition. The mixture was sterilized by autoclaving at 121°C for 15 min **(**Esimone et al., 2010).

Release of extract from the lozenges

Release of extract from the lozenges was evaluated via an *in-vitro* antimicrobial pharmacodynamics protocol**.** A lozenge tablet was placed in a test tube containing 10 ml of sterile saline-saliva solution and shaken throughout the experiment with a mechanical shaker. About 1 ml of the solution was withdrawn in duplicates at time intervals of 5, 10, 20, 30, 60, 120 and 180 min. This was introduced into pre-bored holes in nutrient agar plates previously seeded with a standardized inoculum of bacteria (*S. aureus, S. pyogenes* or *P. aeruginosa*). This was left in the hole for 15 min at room temperature (to allow for pre-diffusion of extracts) and later incubated for 24

Table 2. Weight uniformity test for *A. paniculatus* formulated lozenges and the Standard Stepsils®.

Lozenges	Batch 1	Deviation (%)	Batch 2	Deviation (%)	Strepsils	Deviation (%)
1	1000	0.4	1950	0.2	2250	0.1
2	995	-0.1	2000	3.6	2245	0.1
3	995	-0.1	2000	3.6	2240	0.3
4	1000	0.4	1955	0.6	2250	0.1
5	990	-0.6	1950	0.2	2245	0.1
6	990	-0.6	1900	-3.2	2250	0.1
7	1000	0.4	1900	-3.2	2,245	0.1
8	1000	0.4	2010	4.4	2250	0.1
9	1000	0.4	1900	-3.2	2250	0.1
10	990	-0.6	1900	-3.2	2250	0.1
Total weight	9960		19465		22475	
Mean weight	996		1946.50		2247.50	

Table 3. Hardness and friability tests for lozenges formulated with *A. paniculatus* (25 mg).

Lozenges	Hardness test (Kgf)	Friability test		
	Batch 1	Weight (0)-mg	Weight (1)-mg	Weight loss (%)
1	11.5	1000	995	0.5
2	9.0	995	993	0.2
3	10.5	995	994	0.1
4	10.0	1000	997	0.3
5	11.5	990	989	0.1
6	11.0	990	988	0.2
7	10.5	1000	998	0.2
8	9.5	1000	999	0.1
9	10.0	1000	998	0.2
10	10.5	990	980	0.7
Mean	10.4			

h at 37°C. A fresh normal saline-saliva mixture was similarly introduced into appropriate hole as a negative control. The zones of inhibition were observed visually and measured. This procedure was conducted in duplicate and the mean inhibition zone diameter recorded. The referenced drug-strepsils® was subjected to same physicochemical studies and drug release tests where the IZDs were recorded **(**Esimone et al., 2009**)**.

RESULTS AND DISCUSSIONS

Weight variation, friability, hardness and microbial sensitivity (release time) studies (using three pathogenic bacteria) were conducted on two Lozenges formulated 25 mg (batch 1) and 50 mg (batch 2) and a reference standard, Strepsils^{R}, containing Amylmetacresol (0.6 m) and 2,4-dichlorobenzyl alcohol (2 mg).

The result of the *A. paniculatus* formulated and standard Strepsils® lozenges weight uniformity test was as shown in Table 2. The results showed that the average weights of the batch 1 (25 mg), batch 2 (50 mg) and standard strepsils® lozenges were 946, 1446.50 and 2567.50 mg respectively. The percentage weight deviation of all ten formulated and standard lozenges were found to be within limits (±5 %) with the highest percent variation of -0.1 to 0.4%, 3.6 to 4.4% and 0.1 to 0.3 % for batches 1 and 2 and standard lozenge respectively. All the lozenges were thus found to comply with or passed the weight uniformity test (Indian Pharmacopoeia, 2010) which states that not more than two of individual weights should deviate from the average by more than 5% and none should deviate by more than twice that percentage for tablets weights above 375 mg. It also indicated that ingredients were accurately weighed, and well blended and content uniformity guaranteed.

The result of the standard and formulated lozenges hardness and friability tests were as shown in Tables 3 and 4. The result of the friability test indicated that the percentage weight loss for batches 1 and 2 were found to be between 0.1 to 0.7% and 0.06 to 0.6% respectively

Table 4. Hardness and friability tests for Lozenges formulated with *A. paniculatus* (50 mg).

Lozenges	Hardness test (Kgf)	Friability test		
	Batch 2	Weight (0)	Weight (1)	Weight loss (%)
1	13.5	1950	1949	0.06
2	10.8	2000	1990	0.6
3	12.5	2000	1995	0.3
4	14.5	1955	1950	0.3
5	10.8	1950	1947	0.2
6	13.0	1900	1898	0.1
7	14.0	1900	1899	0.07
8	14.0	2000	1999	0.06
9	14.5	1900	1898	0.1
10	13.0	1900	1898	0.1
Mean	13.1			

Table 5. Hardness and friability tests for standard strepsils®.

Lozenges	Hardness test (Kgf)	Friability test		
	Strepsils®	Weight (0)	Weight (1)	Weight loss (%)
1	15.55	2250	2240	0.39
2	15.55	2245	2240	0.19
3	15.50	2240	2230	0.39
4	15.55	2250	2245	0.19
5	15.60	2245	2225	0.8
6	15.60	2250	2235	0.6
7	15.50	2245	2225	0.8
8	15.55	2250	2240	0.39
9	15.55	2250	22400	0.39
10	15.55	2250	2240	0.39
Mean	15.55			

which were less than 1% indicating that the friability is within prescribed limits (Indian Pharmacopoeia, 2010). This implied that the lozenges have the requisite ability to withstand abrasion during packaging, handling and shipping as a maximum weight loss of not more than 1% is generally considered acceptable.

The result of the crushing strength indicated the crushing strength recorded for batch 1 (10.4 Kgf) was lower than batch 2 (13.1 Kgf). The high concentration of the *A. paniculatus* extract could have been responsible to the higher crushing strength of batch 2 lozenges due to its sticky (polymer) and gummy property as the extract content of this batch was doubled that of batch1 lozenge tablet.

The result of the crushing strength and the friability tests of the standard strepsils® lozenges were recorded as 21.5 Kgf and between 0.19 and 0.8% respectively as shown on Table 5. Based on the above values, it indicated that all the ten lozenge tablets evaluated complied with Indian Pharmacopoeia industrial standards. These physical attributes contribute to ease of use of the lozenge in the mouth to contribute the desired slow dissolution as well as could withstand abrasion during packaging, handling and shipping (Renuka et al., 2014).

The result of the *in vitro* antibacterial susceptibility testing of *Adenodolichos paniculatus* root extract formulated lozenge tablets obtained were as shown in Figures 1 and 2. There was inhibition of growth of *Streptococcus pyogenes, Staphylococcus aureus* and *Pseudomonas aeruginosa* for batch 1 starting from 30 mins and recorded peak inhibition zone within 60-120 mins with inhibition zone diameters of 18.0, 23.0, 24.5 and 18.5; 16.5, 19.5, 21.5 and 16.00; and 9.0, 10.0, 12.0 and 8.0 mm respectively. There was inhibition of growth of *Streptococcus pyogenes, Staphylococcus aureus* and *Pseudomonas aeruginosa* for batch 2 starting from 60 mins and recorded peak inhibition zone at 120 mins with inhibition zone diameters of 24.5, 26.5 and 22.0; 21.5, 23.0 and 20.0; and 11.0, 13.0 and 10.0 mm respectively. There was inhibition of growth of *Streptococcus pyogenes, Staphylococcus aureus* and *Pseudomonas aeruginosa* for Strepsils starting from 5 mins and recorded peak inhibition

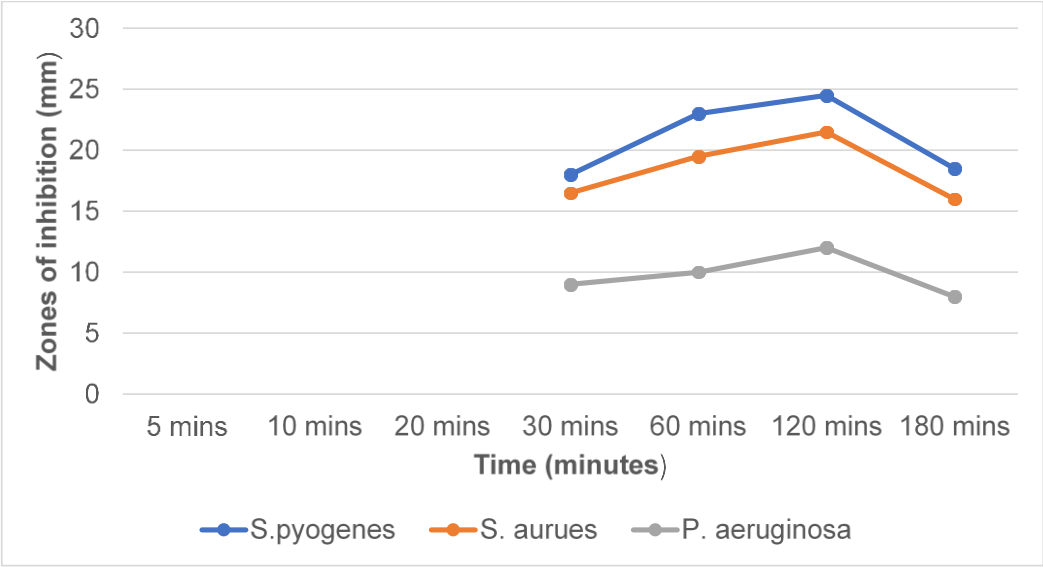

Figure 1. Antibacterial activity of chloroform root extract lozenge tablet, 25 mg.

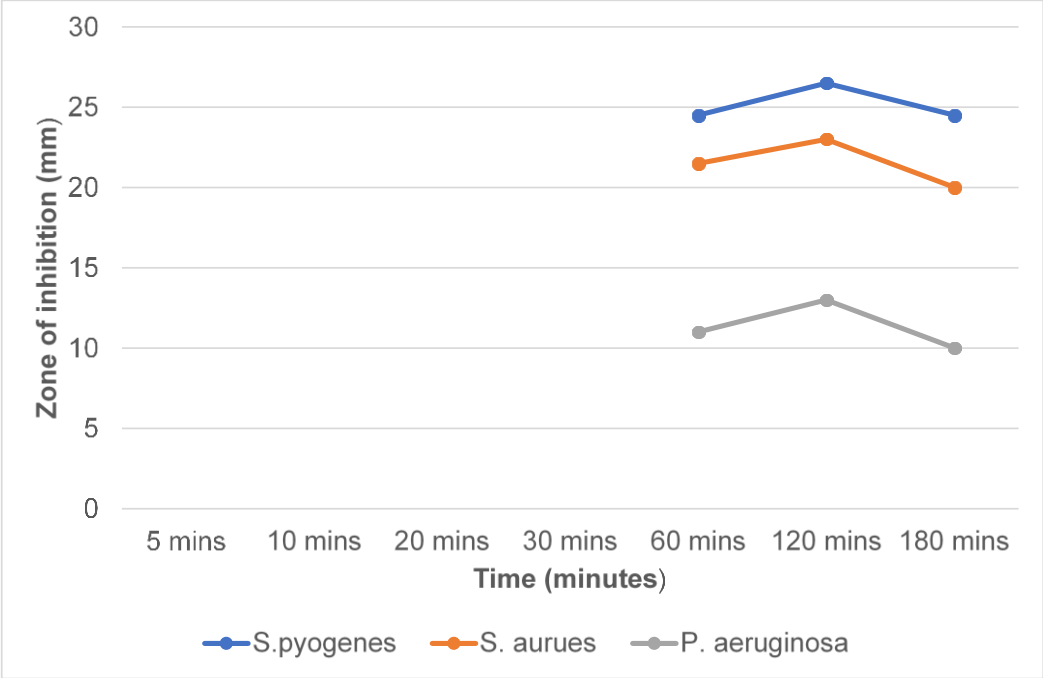

Figure 2. Antibacterial activity of chloroform root extract lozenge tablet, 50 mg.

zone between 20-120 mins with inhibition zone diameters of 25.0, 26.0, 27.5, 27.5, 28.5, 28.5 and 24.0; 19.0, 19.5, 20.0, 22.0, 23.5, 24.0 and 18.0; and 9.0, 9.0, 10.0, 11.0, 13.0, 15.0 and 9.0 mm respectively. The test lozenges tablets were active against each test bacteria. The bacterial susceptibility to the test lozenges tablets compared favorably with the standard formulation, Strepsils as the difference between the inhibition zone diameters of each test bacteria and the standard formulation, Strepsils was not statistically significant ($p>0.05$).

The progressive increase in the size of the inhibition zone diameters noticed in both batches of formulated lozenges tablets with increasing times (30-180 min, batch 1) and (60-180 min, batch 2) was an indicative of a good correlation between extent of release of the *A. paniculatus*

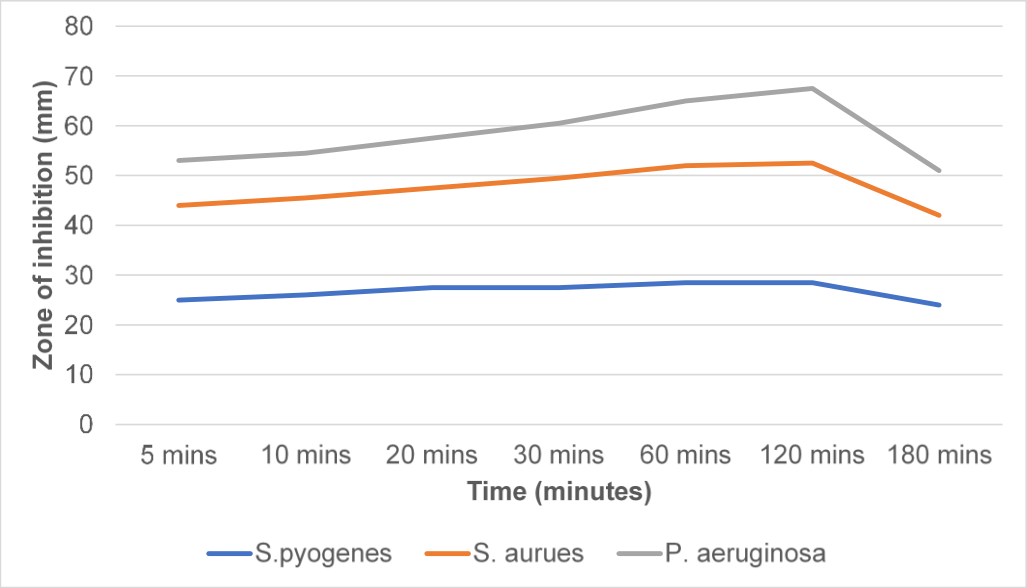

Figure 3. Antibacterial activity of referenced formulation, Strepsils® lozenge tablet.

extract and antibacterial activity. The result indicated that there was a delayed release of the extract from both formulated lozenges with batch 1 being from 30 minutes and batch 2 from 60 minutes compared to that of the standard strepsils® lozenges which had immediate drug released at 5 minutes (Figure 3). The extract release time from lozenge 25 mg was 30 mins, lozenge 50 mg was 60 mins and the standard drug release time was 5mins.

Previous reports on the antibacterial studies properties of *Adenodolichos paniculatus* have shown it to be active against bacterial pathogens such as *S. pyogenes*, *S. aureus*, *P. aeruginosa* which are implicated in oropharyngeal infections (Isyaku, 2018; Kyahar et al., 2021). Not many studies have been reported on the development and antibacterial properties of lozenge formulated with *Adenodolichos paniculatus* extract. However, it has been reported from the study of *in vitro* evaluation of lozenges containing extracts of roots of *Zapoteca porporicensis,* Family: Fabaceae (Esimone et al., 2009) that the formulated lozenges demonstrated antibacterial activities on *S. aureus*. It has been reported from the study on development and evaluation of novel lozenges containing *Marshmallow* root extract (Benbassat et al., 2013) that over 80% of the extract was released at 30 minutes time. It has also been reported (Adedokun and Chukwubuzor, 2014) from the study on antimicrobial evaluation of lozenges formulated with ethanolic extract of *Vernonia amygdalina* that the extract which was found active on *Staphylococcus aureus* remained active on the bacteria after incorporating it into lozenges formulation. It has also been reported (Esimone et al., 2010) from the study on antimicrobial evaluation of lozenges containing extract of garlic and ginger that the formulated lozenges showed inhibitory activity against *C. albicans*, *S. aureus* and *E. coli* infections thus proving a very good release matrix for the garlic-ginger combined extract.

This implied that the method used for the formulation and sticky and gummy nature of the extract might not have allow and promote the release of the antibacterial extract from the dosage form. This accounted for why batch 2 lozenges had the highest delayed time to release the drug probably due the high concentration of the drug extract which was very sticky and gummy in nature thus providing a poor release matrix. Because of gummy property of the extract, it formed a gel layer which might have appeared to restrict or delay immediate permeation of fluid (Obitte, 2001).

Conclusion

On comparison with the referenced formulation result, it could be concluded that the formulation of *Adenodolichos paniculatus* extract into lozenge tablet was a convenient drug form (lozenge) for local delivery of the antibacterial extract for treatment of sore throat infections caused by any of the test bacteria. This is because the bacterial susceptibility to both lozenges tablets compared favorably with the referenced formulation, Strepsils as the difference between the inhibition zone diameters of each test bacteria and the referenced formulation, Strepsils was not statistically significant ($p>0.05$) and the significant difference in release time of the active ingredients between the lozenge tablets and the referenced formulation, Strepsils observed might be

improved upon through more research on the formulation method.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

Adedokun, O. M., & Chukwubuzor, O. P. (2014). *Antimicrobial Evaluation of Lozenges Formulated with Ethanolic Extract of Vernonia amygdalina. World Journal of Pharmacy and Pharmaceutical Sciences*, 3(12), 1785-1794.

Ali, A. I., Ehinmidu, J. O., & Ibrahim, Y. K. E. (2011). *Preliminary Phytochemical Screening and Antimicrobial Activities of some Medicinal Plants used in Ebiraland*. *Bayero Journal of Pure and Applied Sciences*, 4(1), 10-16.

Banu, K. S., & Catherine, L. (2015). General techniques involved in phytochemical analysis. *International Journal of Advanced Research in Chemical Sciences*, 2(4), 25-32

Benbassat, N., Kostova, B., Nikolova, I., & Dimitar Rachev, D. (2013). *Development and Evaluation of Novel Lozenges containing Marshmallow root Extract*. *Pakistan Journal of Pharmaceutical Sciences*, 26(6), 1103-1107.

Dar, R. A., Shahnawaz, M., & Qazi, P. H. (2017). General overview of medicinal plants: A review. *The Journal of Phytopharmacology*, 6(6), 349-351.

Deepika, M., Aparna, C., & Srinivas, P. (2014). *Formulation, evaluation and characterization of itraconazole lozenges. Journal of Pharmacy and Biological Sciences*, 9(3), 86-94.

Esimone, C. O., Ebebe, I. M., Chah, K. F., & Onyeka, C. G. (2003). Comparative antibacterial effects of Psidium guajava aqueous extract. *Journal of Tropical Medicinal Plants*, 4(2), 185-190.

Esimone, C. O., Okoye, F. B. C., Odimegwu, D. C., Nworu, C. S., Oleghe, P. O., & Ejogha, P. W. (2010). *In vitro* antimicrobial evaluation of lozenges containing extract of garlic and ginger. *International Journal of Health Research*, 3(2), 105-110.

Esimone, C. O., Onuh, P. U., Obitte, N. C., Egege, M. K., & Ugoeze, K. C. (2009). *In vitro* evaluation of Lozenges containing extracts of roots of Zapoteca portoricensis (FAM: Fabaceae). *Journal of Pharmacology and Toxicology*, 4(3), 132-137.

Hutchinson, J., & Dalziel, J. M. (1958). Caesalpiniaceae, Mimosaceae and Papilionaceae. *Flora of West Tropical Africa*, 1(2), 439-587.

Indian Pharmacopoeia (2010). The Controller of Publication, Ministry of Health and Family Welfare, India. Pp. 751-754.

Isyaku, I. (2017). Isolation, characterization and antimicrobial activity of bioactive constituents from the leaf extract of *Adenodolichos paniculatus*-unpublished Master Thesis, Ahmadu Bello University, Zaria.

Kyahar, I. F., Onwuliri, A. E., Ehinmidu, J. O., & Oladosu, P. O. (2021). Time-kill kinetics and antibacterial activities of root extracts of *Adenodolichos paniculatus*. *Journal of Pharmacy and Bioresources*, 18(2), 1-9.

Nagoba, S. N., Purushotham R. K., and Zakaullah, S. (2011). Formulation of Clotrimazole as lozenge tablet for improved delivery to oral thrush. *Journal of Pharmacy and Biomedical Science*, 12(12), 1-4.

Obitte, N. C. (2001). *In vitro* properties of encapsulated theophylline granules prepared with *Tacca involucrata* starch. M. Pharm Thesis, Pharmaceutical Technology and Industrial Pharmacy, University of Nigeria, Nsukka.

Olaniyi, A.A. (2005). *Essential medicinal chemistry*. 3rd edition. Ibadan Shaneson CI Ltd. Pp: 346-349.

Renuka, P., & Madhusudan, R. Y (2014). *Lozenges formulation and evaluation: A review*. *International Journal of Advances in Pharmaceutical Research*, 5(5), 290-298

Sani, M., Anuka, J., Magaji, I., Yaro, A., Magaji, M., & Sani, Y. (2010). *Evaluation of analgesic and anti-inflammatory activities of the methanolic leaf extract of Adenodolichos paniculatus* (hua). *Nigerian Journal of Pharmaceutical Sciences*, 9(1), 73-80.

Sastry, S. V., Nyshdham, J. R., & Fix, J. A. (2000). Recent technological advances in oral drug delivery: A review. *Pharmaceutical Science Technology of Today*, 3(4), 138-145.

Swarbrick, J., & Boylan, J. C. (2001). *Encyclopedia of pharmaceutical technology (2nd edition)*. New York: Marcel Dekker.