

Ethnomedicinal study and in vitro validation of medicinal plants used for treating Jaundice in Zuru emirate of Kebbi State, Nigeria

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Abstract

Background: For decades, the resident of Zuru emirate have used herbal medicine to treat liver-related diseases including jaundice. Therefore, the present study was designed to investigate and document the herbal medicine used for treating jaundice in Zuru emirate.

Method: Oral interviews and questionnaire were used to document information on medicinal plants, medicinal practices, and demographic profiles of respondents. The medicinal plants that were mentioned were collected, identified, and assigned voucher numbers. The names were further authenticated using www.theplantlist.org and theworldfloraonline.org. Thereafter, the methanol stem bark extracts of three of the most frequently mentioned plants were subjected to in vitro bilirubin degradation assay.

Result: A total of 46 TMPs Traditional medicine practitioners responded and cited 28 medicinal plants and medicinal practices used to treat jaundice. The most frequently mentioned plants were *Erythrina senegalensis* (19.6%) followed by *Cochlospermum planchonii* (13%), and *Anogeissus leiocarpus* (13%). The herbal remedies were prepared using different parts of the plants as boiled juice or powder and mostly taken as juice with pap or fresh raw cow milk. The in vitro bilirubin degradation assay revealed a time-dependent and dose-dependent bilirubin degradation by *Anogeissus leiocarpus* (63.05 %), *Erythrina senegalensis* (46.33%), and *Cochlospermum planchonii* (27.45%).

Conclusion: The present findings revealed the medicinal plants that are used to treat jaundice and the potential jaundice ameliorative effect of these plants may involve bilirubin degradation. Future in vitro and in vivo mechanistic studies should investigate the jaundice ameliorative potency of these plants.

Keywords: Jaundice; Herbal medicine; Zuru; Liver disease; Nigeria; Hepatoprotective

1.0 Introduction

Neonatal hyperbilirubinemia that can result in clinical jaundice characterized by yellowish skin and sclera is the most common cause of hospitalization and morbidity in newborns. In fact, over 60 % of newborns exhibit clinical symptoms or develop neonatal jaundice (Greco et al., 2016). Global indices estimated that about 1.1 million babies would develop hyperbilirubinemia and the majority of these babies would be from sub-Saharan Africa and South Asia (Olusanya et al., 2016). The prevalence of neonatal jaundice admission in Nigeria is relatively high with bilirubin levels >20mg/dl recorded in 26.9% of hospital admissions (Greco et al., 2016). Similarly, 21% (males) and 12% females of newborn hospital admissions in Warri, Nigeria were found to be jaundiced (Chime et al., 2011).

Besides hospitalization and the use of conventional medicine, the majority of the population especially those residing in rural areas of low-income countries rely on medicinal plants and herbal formulations for treatment. Indeed, ethnomedicinal studies have revealed that Nigerians in rural areas depend on herbal medicine for the treatment of liver diseases, viral infections, cancer etc (Abubakar et al., 2020b; Segun et al., 2018). The Zuru emirate is located in Kebbi State in the northwestern part of Nigeria and is highly endowed with medicinal plants that have been used for the treatment of various ailments for decades. Undoubtedly, the residents of the Zuru emirate have for decades relied on herbal medicine for the treatment of jaundice and other liver-related diseases. Therefore, the present study investigated plants used for treating jaundice in the Zuru emirate.

2.0 Experimental Design

Ethnomedicinal survey

The survey was conducted between November 2020 to April 2021 using a questionnaire and oral interviews according to a previously described protocol (Abubakar et al., 2020a). Ethical approval with approval no KSUSTA/FLS/UREC/20-02 was obtained as previously described (Abubakar et al., 2020a). COVID-19 prevention protocols including social distancing and wearing of nose masks were strictly adhered to. The association of traditional medicine practitioners was contacted to provide contacts of traditional medicine practitioners (TMPs) in all the local government areas within the Zuru emirate. In addition, the health information officers also played a role in mobilizing traditional medicine practitioners to participate in the study through their monthly forum meetings where traditional birth attendants and other community helpers undergo training and reorientation. The Zuru emirate is located in the southeastern part of Kebbi state (northwest Nigeria) and lies on longitude 11.916667 and latitude 11.436467 (Caleb et al., 2020). It consists of four (4) local government areas namely; Zuru, Fakai, DankoWasagu, and Sakaba (Fig 1).

Collection and identification plants

The plants identified by the TMPs were collected and the names authenticated, assigned voucher numbers and deposited in the herbarium according to previous method (Abubakar et al., 2020b). Citation frequency

The citation frequency was calculated according to the previously described protocol using the formula $CF = NC/TI$ (Abubakar et al., 2020b).

Preparation of extract

The stem bark of *Erythrina senegalensis*, *Cochlospermum planchonii*, and *Anogeissus leiocarpus* was collected, air dried at room temperature and was ground to coarse particles, 100g of the sample was soaked in 70% methanol for 72h and subsequently concentrated using a rotary evaporator at 400C until the solvent is significantly reduced and further dried in a petri dish under room temperature. Thereafter, the sample was carefully packed and stored in a refrigerator until needed for further use.

In vitro bilirubin degradation assay

The assay was conducted according to a previously described protocol with slight modification (Zhang et al., 2015). Briefly, 20 mg/dl Bilirubin standard was constituted in buffer solution consisting 18.5% 0.1N NaOH, 44.5% albumin, and 37% 0.055M Na_2PO_4 and pH was adjusted to 7.4. Thereafter, various concentrations of the plants' methanol stem bark extracts (100 mg/dl, 50mg/dl, and 25mg/dl) were incubated with the prepared buffer solution for two (2) hours. The buffer component containing 20mg/dl bilirubin standard served as untreated control. The bilirubin concentration was measured at 578nm using a spectrophotometer.

3.0 Results

Demographic profile and citation frequency

A total of 46 TMPs consisting of 14,12,11 and 9 informants from Zuru, Fakai, Danko wasagu and Sakaba, respectively, participated in the study. The demographic profile revealed that 19.6 % of the TMPs were females (Table 1). Whereas, 84.8% of the TMPs inherited the knowledge with 34.8% of the TMPs having over 20 years' experience majorly within the age range of 41-50 years. A total of 28 medicinal plants belonging to 20 families were cited by TMPs for treating jaundice and liver-related diseases in the Zuru emirate (Table 2). *Erythrina senegalensis* (19.6%), *Cochlospermum planchonii* (13%), and *Anogeissus leiocarpus* (13%) were the most frequently mentioned plants. The parts of plants used for preparing different herbal remedies include leaf, stem bark, root, and whole plant. The herbal remedies are prepared as a powder or boiled and taken with local pap, fresh raw cow milk, or as steam.

Diagnosis of jaundice by TMPs

The TMPs use signs and symptoms to diagnose jaundice whereas in most cases they rely on the results of hospital diagnosis of their patient because the majority of the patients get referred to the traditional practitioners through families and acquaintances or through interactive testimonies

In vitro bilirubin degradation

The methanol stem bark extracts of three of the most frequently mentioned plants were assayed for bilirubin degradation potency. *Anogeissus leiocarpus* was the most potent and induced dose and time-dependent bilirubin degradation with $63.05 \pm 0.15 \%$, followed by *Erythrina senegalensis* ($46.33 \pm 0.38 \%$), and *Cochlospermum planchonii* ($27.45 \pm 0.05 \%$) degraded by 100mg/dl of extract after 1.5h (Table 4).

Statistical analysis

The data was analyzed using the post-hoc analysis with turkey's multiple comparison under two-way ANOVA using the SPSS version 20 software. The data with ($p < 0.05$) were considered statistically significant.

4.0 Discussion

The northwestern part of Nigeria and especially the Zuru emirate of Kebbi State continuously treat diseases using herbal medicine recipes. This can be attributed to its affordability and long-term belief in its potency and effectiveness in curing various health problems by the locals. Recent studies have reported that medicinal plants are used to treat diseases including cancer, diabetes, and viral infections in the Zuru emirate and the northwestern part of Nigeria (Abubakar et al., 2022, 2020a). Indeed, the Zuru emirate comprising six major tribes namely Dakarkari, Fakkawa, Dukkawa, Achifawa, Hausa, and Fulani has a long rich history of treating diseases using traditional medicine.

Herein, we investigated and documented medicinal plants used for treating jaundice in the Zuru emirate. *Erythrina senegalensis* was the most frequently mentioned plant with the leaves or stem bark used in preparing various decoctions for oral administration.



Fig 1: Map showing Zuru emirate

Table 1: Demographic profile of TMPs in Zuru emirate

s/no	Parameters	Ranges	Percentage (%)
1	Age (Years)	21-30	6.5
		31-40	15.2
		41-50	34.8
		51-60	28.2
		61-70	13
		71-80	2.2
2	Experience (Years)	0-5	4.3
		6-10	13
		11-20	47.8
		21 and above	34.8
3	Educational status	Primary	6.5
		Secondary	26.1
		Tertiary	2.2
		No formal education	65
4	Gender distribution	Male	80.4
		Female	19.6
5	Source of knowledge	Inherited	84.8
		Acquired	15.2

Table 2: Inventory of medicinal plants used for treating Jaundice by TMPs in Zuru emirate

s/n	Botanical name	Family name	Local name	Common name	Voucher no	Frequency	Plant part	Mode of preparation	Route of administration
1	<i>Annona senegalensis</i> Pers.	<i>Annonaceae</i>	Gwanda daji	Wild custard apple	Ksusta/psb/h/504A	2.2	Root	The root is boiled and a little quantity of salt is added, the extract can then be consumed.	One full cup is taken orally once daily for one week
2	<i>Anogeissus leiocarpus</i> (DC.) Guill. & Perr.	<i>Combretaceae</i>	Marke	African Birch	Ksusta/psb/h/512	13.0	Stembark/leaves	The leaves or stems are boiled and filtered. The filtrate is taken as juice. The stem bark can also be boiled with red potash	A full cup is taken daily for up to one week.
3	<i>Artemisia annua</i> L.	<i>Compositae</i>	Tazargade	Sweet annie	Ksusta/psb/h/112	2.2	Root	The root is boiled	The juice (1/2 cup) is administered orally for 7/12 days.
4	<i>Azadirachta indica</i> A.Juss.	<i>Meliaceae</i>	Darbejiya	Neem	Ksusta/psb/h/61	2.2	Root	The roots are boiled and filtered.	The extract (1/2 cup) is orally administered daily for three days
5	<i>Bridelia ferruginea</i> Benth	<i>Phyllanthaceae</i>	Kizni		Ksusta/psb/h/sn	2.2	stembark	The stem bark is dried and ground to powder.	The powder is mixed with pap and consumed twice daily for one week
6	<i>Calotropis procera</i> (Aiton)	<i>Apocynaceae</i>	Tunfafiya	Sodom apple, rubber bush	Ksusta/psb/h/ 03	10.9	Root	The root is boiled and taken alone or used in making pap, the root can also be dried and crushed to powder.	A full cup in the morning and evening for 3 days or a little quantity of the powder is taken in fresh raw cow milk
7	<i>Carica papaya</i> L.	<i>Caricaceae</i>	Gwanda gida	Pawpaw	Ksusta/psb/h/66a	8.7	Leaf	Decoction	One full cup of pap or quarter of a cup is taken orally once daily for one week
8	<i>Cassia occidentalis</i> (L.) Rose	<i>Fabaceae</i>	Sanga sanga	Coffee senna	Ksusta/psb/h/71	6.5	Whole plant	The plant is boiled.	Hot preparation is used as steam under a covered cloth
9	<i>Cassytha filiformis</i> L.	<i>Lauraceae</i>	Inuwar gada/Rumfar gada	Love vine	Ksusta/psb/h/sn	6.5	leaves	The leaves are boiled and filtered.	The juice (1/2 cup) is orally administered three times daily.
10	<i>Citrus aurantium</i> L.	<i>Rutaceae</i>	Lemu	Orange	Ksusta/psb/h/285	2.2	leaves	The leaves are boiled with water and a small amount of red potash is added and filtered.	The juice (1/2 cup) is orally administered daily for seven (7) days.
11	<i>Cochlospermum planchonii</i> Hook.f. ex Planch	<i>Cochlospermaceae</i>	Kwata		Ksusta/psb/h/232	13.0	Root	The root is boiled and filtered.	The filtrate is administered as juice.
12	<i>Dioscorea bulbifera</i> L.	<i>Dioscoreaceae</i>	Tuwon biri		Ksusta/psb/h/121	4.3	Stem bark	The stem bark is boiled with water and a little quantity of potash or sour orange is added.	One full cup is taken orally twice daily for 3 days
13	<i>Erythrina senegalensis</i> DC.	<i>Fabaceae</i>	Karya	Coral tree	Ksusta/psb/h/114	19.6	Stembark/leaves	1. The stem bark is boiled and little quantity of red potash is added and the juice is taken.	1. Half a cup is taken orally 3 times daily.

								2. The leaves can also be boiled and the extract is used to prepare pap.	2. A cup of pap is taken once daily.
14	<i>Faidherbia albida</i> (Delile) A.Chev	<i>Fabaceae</i>	Gawo	Winter thorn	Ksusta/psb/h/319	2.2	Stem bark	The stem bark is boiled and the filtrate is taken	One full cup morning and evening for three days
15	<i>Ficus thonningii</i> Blume	<i>Moraceae</i>	Chediya		Ksusta/psb/h/511a	4.3	Leaves	The leaves are dried and ground to powder.	The powder is mixed with pap and consumed twice daily for one week
16	<i>Gardenia erubescens</i> Stapf. & Hutch	<i>Rubiaceae</i>	Namijin gaude		Ksusta/psb/h/309a	2.2	Root	The root is dried and ground to powder.	A certain amount of the powder is taken with a half cup of pap.
17	<i>Guiera senegalensis</i> J.F. Gmel	<i>Combretaceae</i>	Sabara	Moshi medicine	Ksusta/psb/h/48	2.2	Leaves	The leaves are dried and ground to powder.	The powder is taken with fresh raw milk twice daily for one week
18	<i>Ludwigia octovalvis</i> (Jacq.) P.H. Raven	<i>Onagraceae</i>	Shashatau	Mexican primrose willow	Ksusta/psb/h/ 517	2.2	Whole plant	The whole plant is boiled and filtered. The filtrate is taken as juice.	A half cup is taken orally once daily for two weeks.
19	<i>Luffa cylindrica</i> (L.) M.Roem.	<i>Cucurbitaceae</i>	Soson bature/Baska	Sponge gourd	Ksusta/psb/h/s.n	2.2	leaves	The whole plant is boiled and a little quantity of red potash is added while boiling.	Half a cup of the extract is taken orally after breakfast.
20	<i>Mangifera indica</i> L.	<i>Anacardiaceae</i>	Mangwaro	Mango	Ksusta/psb/h/63	2.2	Stem bark	The stem bark is boiled and filtered or the stem bark is dried and prepared into powder	The filtrate is taken as juice once daily for one week or the powder is taken in pap twice daily.
21	<i>Momordica charantia</i> L	<i>Cucurbitaceae</i>	Garahuni	Balsam pear	Ksusta/psb/h/s.n	2.2	Whole plant	The whole plant is boiled with little quantity of garlic and the filtrate is taken as juice.	A half cup is taken orally 3 times daily
22	<i>Moringa oleifera</i> Lam.	<i>Moringaceae</i>	Zogala	Moringa	Ksusta/psb/h/132	4.3	Root	The root is boiled and the extract is used to prepare pap.	A filled cup of pap is taken daily for at least days.
23	<i>Piliostigma thonningii</i> (Schum.) Milne-Redh.	<i>Fabaceae</i>	Kalgo	Wild bauhinia	Ksusta/psb/h/109	4.3	Stem bark	The stem bark is dried and ground to powder.	The powder is mixed with pap and consumed twice daily for one week
24	<i>Psidium guajava</i> L.	<i>Myrtaceae</i>	Gwaiba	Guava	Ksusta/psb/h/120b	2.2	leaves	The leaves are dried and ground to powder.	The powder is mixed with pap and consumed
25	<i>Sterculia setigera</i> Delile	<i>Malvaceae</i>	Kukkuki	Karaya gum Tree	Ksusta/psb/h/ 83B	2.2	Stem bark	The stem bark is dried and ground to powder.	A certain amount of the powder is taken with pap twice daily.
26	<i>Tamarindus indica</i> L.	<i>Fabaceae</i>	Tsamiya	Tamarind	Ksusta/psb/h/66	2.2	Stem bark/ root	The leaves are dried and ground to powder.	The powder is mixed with pap or water and consumed twice daily for one week.
27	<i>Terminalia macroptera</i> Guill. & Perr.	<i>Combretaceae</i>	Kandare/kwandar i		Ksusta/psb/h/sn	2.2	Stem bark/ root	The stem bark is dried and crushed to powder.	The powder is taken with fresh raw cow milk twice daily for three days.
28	<i>Vernonia amygdalina</i> Delile	<i>Compositae</i>	Shuwaka	Bitter leaf	Ksusta/psb/h/127b	2.2	Leaves	The leaves are squeezed in water to form juice and filtered.	One full cup of the juice is taken orally once daily for 3 days

Table 3. Ethnomedicinal uses and hepatoprotective/toxicity effect of some of the mentioned plants

s/no	Botanical name	Relevant ethnomedicinal uses	Relevant pharmacological activity	Toxicity
1	<i>Annona senegalensis</i>	To treat yellow fever, tuberculosis, small pox, chicken pox and venomous bites in Nigeria. To treat fever, malaria, alcoholism and kidney sickness in Benin Republic. To treat liver disease in Togo (Adjakpa et al., 2017; Kpodar et al., 2016; Okhale et al., 2016)	The stem bark extract induced hepatoprotective effect against CCl ₄ -induced hepatotoxicity (Omeke et al., 2019)	The LD ₅₀ for oral ethyl acetate root bark extract 2154 mg/kg but there was degeneration and necrosis of hepatocytes at 400mg/kg (Okoye et al., 2012)
2	<i>Anogeissus leiocarpus</i> (DC.) Guill. & Perr.	Used to treat jaundice, hepatitis, yellow fever, typhoid, hypertension, etc. in Africa. Used to treat liver disease in Togo (Kpodar et al., 2016; Singh et al., 2016a)	Methanol extract induced reduction in serum and liver ALT, AST, Bilirubin, protein and albumin levels. Induced <i>in vivo</i> hepatoprotective effect against CCl ₄ -induced hepatotoxicity (Akanbi et al., 2014; Singh et al., 2016a)	Oral aqueous extract did not cause death at 3200 mg/kg but the intraperitoneal route caused toxicity including death with LD ₅₀ at 1400 mg/kg in rats (Singh et al., 2016a)
3	<i>Artemisia annua</i> L	To treat malaria (Mahomoodally and Gurib-fakim, 2013)	Induced potent effect against malaria parasite (Mahomoodally and Gurib-fakim, 2013)	Few adverse effects have been reported in children and pregnant women (Willcox et al., 2011)
4	<i>Azadirachta indica</i> A.Juss.	To treat diabetes in Nigeria, and malaria in Kenya and Cote d'Ivoire (Akbar, 2018)		The LD ₅₀ of oral aqueous extract was < 5000 mg/kg in mice whereas, the LD ₅₀ of intramuscular injection for aqueous leaf and seed extract was 6.2 and 9.4 ml, respectively (Braga et al., 2021)
5	<i>Bridelia ferruginea</i> Benth	To treat liver disease in Togo (Kpodar et al., 2016)	The aqueous leaf extract induced hepatoprotective effect against 2-acetylaminoflourene induced damage in rats (Adetutu and Olorunnisola, 2013)	The LD ₅₀ of oral aqueous stem bark extract was >4000mg/kg in rodents (Awodele et al., 2015)
6	<i>Calotropis procera</i> (Aiton)	The latex is used in combination with other herbs to treat fever, rheumatism, indigestion and diarrhea in Nigeria. It is used in Indian medicine to treat the liver. Roots and shoots are mixed with <i>Phyllanthus amarus</i> leaves in form of paste and oral administration for the treatment of jaundice in Pakistan (Azhar et al., 2014; Upadhyay, 2014)	The root bark extract exhibits hepatoprotective effect against paracetamol-induced hepatitis in rats (Meena et al., 2011)	The latex is toxic and has been used to prepare poison and the plant is not consumed by grazing animals (Parihar and Balekar, 2016)
7	<i>Carica papaya</i> L	To treat liver disease in Togo (Kpodar et al., 2016). The unripe fruit and leaf are used to treat Jaundice, hypertension, diabetes and malaria by the Yoruba tribe in Southwest Nigeria whereas, the unripe fruit is used to treat Ulcer in Southeast Nigeria (Hainida et al., 2015)	Possess hepatoprotective effect against CCl ₄ and ethanol-induced liver injury in rats (Dotto and Abihudi, 2021)	Oral administration of extract up to fourteen times the dose used in traditional medicine did not cause any significant toxic effect in rats (Afzan et al., 2012)
8	<i>Cassia occidentalis</i> (L). Rose	To treat liver disease in Togo, Viral hepatitis A & C and liver damage. Roots are boiled and taken as a tea to treat constipation in Nigeria (Kpodar et al., 2016; Yadav et al., 2010)	The leaf extract induced significant hepatoprotection against paracetamol and ethyl alcohol-induced liver damage in rats (Yadav et al., 2010)	Consumption of the seeds is associated with hepatomyoencephalopathy in children in India (Panigrahi et al., 2014)
9	<i>Cassytha filiformis</i> L	To treat hepatitis. Used to treat jaundice in Nigeria (Adamu et al., 2017; Raj et al., 2013)	The methanol extract induced hepatoprotective effect against CCl ₄ induced hepatotoxicity in rats (Raj et al., 2013)	The LD ₅₀ of the aqueous whole plant extract is greater than 500mg/kg (Babayi et al., 2007)

10	<i>Citrus aurantium</i> L.	The juice is mixed with bicarbonate of soda and administered orally to treat liver ailments in Haiti. It is used to as hepatoprotective medicinal food in Persian medicine (Memariani et al., 2020; Paul and Cox, 1995)	Antidiabetic and antiulcer effect (Suntar et al., 2018)	A clinical study showed that <i>C. aurantium</i> and its <i>p</i> -synephrine did not cause any adverse cardiovascular effect on 16 individuals after 15 days treatment (Suntar et al., 2018)
11	<i>Cochlospermum planchonii</i> Hook.f. ex Planch	The plant is used to treat jaundice and hepatic fever in northern Nigeria (Anaga and Oparah, 2009)	Extract inhibited CCl ₄ induced hepatotoxicity (Aliyu et al., 1995)	A dose of 50-250mg/kg of aqueous root extract for seven days is not recommended as a safe dose for the herbal remedy as evident in mice (Nafiu et al., 2013)
12	<i>Dioscorea bulbifera</i> L	Used in treating diabetes and ulcer (Ikiriza et al., 2019)	Antinociceptive and anti-inflammatory activities (Guan et al., 2017)	The LD ₅₀ for intraperitoneal and oral administration of the extract are 25.49 g/kg and 79.98 g/kg (Guan et al., 2017)
13	<i>Erythrina senegalensis</i> DC.	Leaves, roots and bark are used to treat jaundice in Mali (Togola et al., 2008)	The stem bark induced antihypertensive and antidiabetic effects on diabetic hypertensive rats (Claude et al., 2020)	Acute and sub-chronic studies in rodents demonstrated that there is a wide safety margin for the therapeutic use of stem bark extract (Atsamo et al., 2011)
14	<i>Faidherbia albida</i> (Delile) A.Chev	To treat diarrhea, dysentery, fever hemorrhages in West African medicine (Nyambe et al., 2021)	Induced anti-hyperglycemic and anti-hyperlipidemic effects in alloxan-induced diabetic rats (Umar et al., 2014)	Relatively safe (Nyambe et al., 2021)
15	<i>Ficus thonningii</i> Blume	The leaf is used to treat gastritis and gastric ulcer in Nigeria. The leaf is also used to treat liver disorders and jaundice. The root is used to treat hepatitis (Dangarembizi et al., 2013)	Antiulcer, renal-protective and cardio-protective effects (Musabayane et al., 2009)	The LD ₅₀ for oral and intraperitoneal administration are > 3000mg/kg and 584mg/kg (Dangarembizi et al., 2013)
16	<i>Gardenia erubescens</i> Stapf. & Hutch	The roots and bark is used to treat gonorrhea and abdominal disorders in Northern Nigeria. The bark is used to treat yellow fever in Burkina Faso (Dramane et al., 2019; Hussain et al., 1991)		There was no sign of toxicity following oral administration of 2000mg/kg of ethanol extract in mice (Dramane et al., 2019)
17	<i>Guiera senegalensis</i> J.F. Gmel	To treat diarrhea, dysentery, fever and diabetes in Nigeria. Used to treat jaundice in Sudan (Dirar and Devkota, 2021)	Induced hepatoprotective effect (Dirar and Devkota, 2021)	The LD ₅₀ for aqueous root extract is > 5000mg/kg for oral administration and 1264.9±250mg/kg for intraperitoneal (Dirar and Devkota, 2021)
18	<i>Ludwigia octovalvis</i> (Jacq.) P.H. Raven	To treat nephritis, diabetes and hypertension (Kadum Yakob et al., 2012)	Induced hepatoprotective and cardioprotective effect (Lin et al., 2014)	Administration of 200-800mg/kg/day of 80% methanol extract did not cause lethality or toxic effect (Kadum Yakob et al., 2012)
19	<i>Luffa cylindrica</i> (L.) M.Roem.	To treat diabetes in Egypt and as an emollient in Nigeria (Akinwumi et al., 2021)	The methanol leaf extract induced hepatoprotective effect against paracetamol-induced liver injury (Sharma et al., 2014)	Administration of 4000mg/kg methanol leaf extract did not cause death or toxic effect in Swiss albino rat (Akinwumi et al., 2021)
20	<i>Mangifera indica</i> L.	The bark is used to treat jaundice in Bangladesh and India. The leaf decoction is used to treat diabetes and malaria in Nigeria (Ediriweera et al., 2017)	Pulp extract combined with lupeol Induced hepatoprotective effect against 7, 12-dimethylbenzanthracene induced liver alteration in Swiss albino mice (Shah et al., 2010)	Studies have reported the lack of toxic effect although minimal toxic effect on seed kernel has been reported (Derese et al., 2017)

21	<i>Momordica charantia</i> L.	It is used to treat jaundice in India. It is also used to treat hepatitis (Grover and Yadav, 2004)	Hydroalcoholic leaf extract induced hepatoprotective effect against CCl ₄ induced hepatotoxicity in rats (Moharir et al., 2019)	The plant is relatively safe as no toxicity is reported in experimental animals when administered at low dose for up to 2 months (Grover and Yadav, 2004)
22	<i>Moringa oleifera</i> Lam.	To treat liver disease in Togo. The pods are used to treat diarrhea, liver and spleen problems (Gopalakrishnan et al., 2016; Kpodar et al., 2016)	The methanol leaf extract as well as the aqueous and alcohol flower extracts induced hepatoprotective effect (Anwar et al., 2007)	Administration of 6400mg/kg of the aqueous extract did not cause mortality (Rani et al., 2018)
23	<i>Piliostigma thonningii</i> (Schum.) Milne-Redh.	The leaf is used to treat malaria in eastern Nigeria. Used to treat dysentery, gonorrhea and ulcer (Cyril et al., 2021)	The extracts induced hepatoprotective effect (Cyril et al., 2021)	The LD ₅₀ of aqueous leaf extract is 10g/kg (Cyril et al., 2021)
24	<i>Psidium guajava</i> L.	To treat liver disease in Togo (Kpodar et al., 2016)	The aqueous leaf extract at 500mg/kg induced significant hepatoprotective effect against carbon tetrachloride induced liver damage (Gutiérrez et al., 2008)	The LD ₅₀ of guava leaf extract is more than 5g/kg in rat and mice (Gutiérrez et al., 2008)
25	<i>Sterculia setigera</i> Delile	To treat Jaundice (Babalola et al., 2012)	Stem bark extract induced hepatoprotective effect against acetaminophen induced hepatotoxicity in rats (Garba et al., 2018)	The aqueous stem bark extract did not significantly change biochemical parameters in Wistar rats (Zaruwa et al., 2016)
26	<i>Tamarindus indica</i> L.	To treat jaundice and yellow fever in Nigeria as well as hepatitis A in Guinea-Bissau (Havinga et al., 2010)	The leaves showed liver protective effect against acute alcohol induced liver toxicity (Kuru, 2014)	Animal feed containing <i>T. indica</i> seed extract did not cause any toxic effect over a period of two years (Kuru, 2014)
27	<i>Terminalia macroptera</i> Guill. & Perr.	To treat hepatitis in Mali. Used to treat liver diseases in Burkina Faso, Mali, Senegal, and Guinea-Bissau (Haidara et al., 2020; Thu et al., 2011)	The leaf and root extract demonstrated hepatoprotective effect (Haidara et al., 2020)	The LD ₅₀ for methanol leaf extract was more than 5000mg/kg in mice (Ior et al., 2020)
28	<i>Vernonia amygdalina</i> Delile	To treat typhoid fever and yellow fever in Nigeria, liver disease in west Africa, hepatitis in Rwanda and jaundice in Cameroon (Oyeyemi et al., 2018; Yeap et al., 2010)	The methanol leaf extract induced hepatoprotective effect against CCL ₄ induced hepatotoxicity in rats (Adesanoye and Ã, 2010)	Administration of aqueous (1200mg/kg) and ethanol (2000mg/kg) extract for 28 days did not cause toxic effect in mice (Oyeyemi et al., 2018)

Table 4: *In vitro* bilirubin degradation assay

Extracts / Concentrations	Time	Bilirubin concentration (mg/dl)			
		100	50	25	control
<i>Erythrina senegalensis</i>	30 min	28.15±0.05 ^{d*}	18.00±0.20 ^{c*}	8.75±0.10 ^{b*}	0.00±0.00 ^{a*}
	60 min	35.60±0.10 ^{d**}	26.08±0.23 ^{c**}	19.53±0.03 ^{b**}	0.00±0.00 ^{a*}
	90 min	46.33±0.38 ^{d***}	36.00±0.40 ^{c***}	28.68±0.23 ^{b***}	1.50±0.00 ^{a*}
<i>Cochlospermum planchonii</i>	30 min	12.33±0.46 ^{d*}	9.50±0.50 ^{c*}	4.03±0.08 ^{b*}	0.00±0.00 ^{a*}
	60 min	21.53±0.18 ^{d**}	11.58±1.03 ^{c**}	8.63±0.28 ^{b**}	0.00±0.00 ^{a*}
	90 min	27.45±0.05 ^{d***}	20.50±0.10 ^{c***}	9.40±0.55 ^{b**}	1.50±0.00 ^{a*}
<i>Anogeissus leiocarpus</i>	30 min	37.33±1.33 ^{d*}	27.75±0.00 ^{c*}	19.00±0.10 ^{b*}	0.00±0.00 ^{a*}
	60 min	50.80±0.30 ^{d**}	42.78±0.43 ^{c**}	28.03±0.08 ^{b**}	0.00±0.00 ^{a*}
	90 min	63.05±0.15 ^{d***}	55.00±0.10 ^{c***}	40.50±0.10 ^{b***}	1.50±0.00 ^{a*}

Values are expressed as Mean ± Standard Error of Mean (SEM). Values with different alphabet in superscript across the row are statistically different (p<0.05) while values with different numbers of * down the columns are statistically different (p<0.05) after post-hoc analysis using turkey's multiple comparison under two-way ANOVA

Interestingly, a previous Ethnomedicinal study revealed that the root and bark are also used to prepare oral herbal remedies including decoctions, maceration, powder, and infusion for treating jaundice in Mali in agreement with the present study (Togola et al., 2008). *Cochlospermum planchonii*, the second most frequently cited plant, is reportedly used to treat jaundice and hepatic fever in northern Nigeria (Anaga and Oparah, 2009). Similarly, *Anogeissus leiocarpus* cited herein is also reportedly used to treat jaundice and other liver-related diseases such as yellow fever, typhoid fever, and hepatitis in other African countries (Singh et al., 2016b). Likewise, *Calotropis procera* is used to treat liver disease in India whereas its shoot and root are mixed with *Phyllanthus amarus* leave in the form of paste for treatment of jaundice in Pakistan. Contrarily the latex is mixed with other herbs and used to treat fever, diarrhea, and rheumatism in other parts of Nigeria (Azhar et al., 2014; Upadhyay, 2014). In addition, *Carica papaya* is used to treat liver disease in Togo whereas its unripe fruit and leaf are used to treat jaundice by the Yoruba tribe in Southwest Nigeria thus agreeing with the reported use in the present study (Hainida et al., 2015; Kpodar et al., 2016). The present study is also in agreement with previous ethnomedicinal studies that reported the use of *Tamarindus indica* (Nigeria), *Vernonia amygdalina* (Cameroun), *Guiera senegalensis* (Sudan), and *Mangifera indica* (Bangladesh and India) for the treatment of jaundice in various countries (Dirar and Devkota, 2021; Ediriweera et al., 2017; Havinga et al., 2010; Oyeyemi et al., 2018; Yeap et al., 2010). Relatively, *Ficus thonningii* and *Sterculia setigera* are used to treat jaundice and other liver-related diseases (Babalola et al., 2012; Dangarembizi et al., 2013). However, to the best of our knowledge, some of the medicinal plants reported herein have not been reportedly used to specifically treat jaundice nonetheless, these plants have been used to treat liver-related diseases. For instance, *Annona senegalensis* and *Bridelia ferruginea*, *Cassia occidentalis*, *Moringa oleifera*, and *Psidium guajava* are used to treat liver diseases in Togo (Kpodar et al., 2016). Similarly, *Terminalia macroptera* is used to treat hepatitis and liver-related diseases in Burkina Faso, Mali, Senegal, and Guinea-Bissau (Haidara et al., 2020; Thu et al., 2011). In addition, to the best of our knowledge, there are medicinal plants cited herein that are reportedly used to treat non liver diseases. For instance, *Azadirachta indica*, *Dioscorea bulbifera*, *Faidherbia albida*, *Ludwigia octovalvis*, *Luffa cylindrica*, *Piliostigma thonningii* are used to treat diseases such as diabetes, dysentery, fever, malaria, etc (Table 3). Therefore, the present study is the first to report the use of these plants for the treatment of jaundice.

On the other hand, biological activity studies on these plants reported several activities including hepatoprotective activity. For example, *Annona senegalensis*, *Anogeissus leiocarpus*, *Carica papaya*, *Psidium guajava*, *Cochlospermum planchonii*, and *Vernonia amygdalina* induced hepatoprotective activity against CCl₄ induced hepatotoxicity (Adesanoye and Å, 2010; Akanbi et al., 2014; Aliyu et al., 1995; Dotto and Abihudi, 2021; Gutiérrez et al., 2008; Omeke et al., 2019). Similarly, *Calotropis procera*, *Cassia occidentalis*, *Luffa cylindrica*, *Sterculia setigera* were hepatoprotective against paracetamol-induced liver toxicity (Garba et al., 2018; Meena et al., 2011; Sharma et al., 2014; Yadav et al., 2010). Furthermore, as shown in Table 3 there are plants cited herein that also induced hepatoprotective effect against various types of induced liver toxicity. This suggest that the majority of the plants cited herein have the potency against liver-related diseases that may include jaundice. However, there is a need for further studies to investigate the in vitro bilirubin degradation potency and in vivo jaundice ameliorative effect of the plants. Medicinal plants and natural products are considered safe with fewer side effects compared to synthetic compounds. However, toxicity has also been associated with medicinal plants. For instance, the latex of *Calotropis procera* cited herein is reportedly toxic and has been used to prepare poison whereas, the plant is avoided by grazing animals (Parihar and Balekar, 2016). Likewise, consumption of the seeds from *Cassia occidentalis* has been reportedly associated with hepatomyoencephalopathy in children in India (Panigrahi et al., 2014). Contrarily, as shown in Table 3, the majority of the plants are relatively safe at appropriate low doses. In fact, various extracts from plants including *Azadirachta indica*, *Guiera senegalensis*, *Psidium guajava*, and *Terminalia macroptera* have oral LD50 above 5000mg/kg (Braga et al., 2021; Dirar and Devkota, 2021; Gutiérrez et al., 2008; Ior et al., 2020).

The inability of the liver of newborns to rapidly clear bilirubin from the blood can result in a toxic hyperbilirubinemia that can affect the central nervous system and eventually result in neonatal jaundice (Mwaniki et al., 2012). Herein, we investigated the in vitro bilirubin degradation potency of three of the most cited plants in the present study. The results revealed dose-dependent and time-dependent bilirubin degradation with the most potent effect evident for *Anogeissus leiocarpus* (63.05 %) followed by *Erythrina senegalensis* (46.33%), and *Cochlospermum planchonii* (27.45%) following 90 min incubation compared to untreated control. Therefore, this suggests that the potential jaundice ameliorative effect of these plants may

involve bilirubin degradation. However, further in vivo and mechanistic studies are required to establish the potency and potential mechanism of action of these medicinal plants.

Conclusion

The present study revealed medicinal plants used to treat jaundice in Zuru emirate some of which have been reported elsewhere for the same medicinal purpose. The study also revealed new plants used for treating jaundice. Furthermore, the potential jaundice ameliorative effect of some of the plants may involve bilirubin degradation. Therefore, further in vitro and in vivo mechanistic studies should be conducted to establish the potency of these plants and provide further scientific justification on the use of these medicinal plants for the treatment of jaundice.

Conflict of interest

The authors declare that there are no conflict interests

Authors Contribution

JBD, IBA, JN Conceptualize the work

AM, IM, IBA, JBD Designed the research

JBD conducted the field work and experimental analysis

JBD, IBA, JN, AA analyzed and interpreted the data

JBD, IBA, JN, AM, IM, AA wrote and proofread the manuscript

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