Review Article

A review on the Phytochemistry and Pharmacological properties of *Picralima nitida* Durand and H. (Apocynaceae family): A potential antiCovid-19 medicinal plant species

Clément Liyongo Inkoto, Jean-Pierre Kayembe Kayembe, Pius Tshimankinda Mpiana, Koto-te-Nyiwa Ngbolua

Abstract

In this mini-literature review, the traditional use, nutritional value, phytochemistry and biological properties of *P. nitida*, a plant used as a conventional African medicine is described. The literature discussed in this investigation established that extracts from *P. nitida* were very efficient in the treatment of several diseases including malaria. Hence we anticipate that it may be effective against Covid-19 virus also. We suggest that in vitro and in vivo assays should be conducted to confirm the activity of the plant against SARS-CoV-2.

Keywords covid-19, medicinal plant, *Picralima nitida*, phytochemistry, pharmacological activities

Introduction

The world is confronted with a new coronavirus epidemic called COVID-19. This novel incipient disease is initiated by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. A genetic study has revealed that SARS-CoV-2 belongs to the Beta coronavirus family and is very similar to SARS-CoV-1 [1]. Despite the biosafety and hygiene measures to limit the large-scale spread of this pandemic, there is currently no antiCovid-19 drug approved by the World Health Organization (WHO). Therefore, traditional medicines can play a pivotal role in the management of this pandemic. Indeed, medicinal plants have been used in folk medicine for generations in most of the cultures throughout the world and are the primary form of treatment in many areas today [2]. However, among the 250,000-500,000 species of plants on earth, only a relatively small percentage (1-10 %) is used for food by humans and animals [3]; however, more may serve medicinal purposes. Medicinal plants are an important source of molecules with various pharmacological properties. These medicinal values of plants have been claimed to lie in their phytochemical components including alkaloids, tannins, flavonoids, and other phenolic compounds [4]. According to the World Health Organization, more than 80% of the population in Africa uses traditional medicine to solve the primary health problems. The traditional medicines have the advantage of being safe, effective, less expensive, and less risky, with significantly reduced side effects compared to modern medicines [5-9]. *Picralima nitida* Durand
and H. (Apocynaceae family) is widely distributed in the high deciduous forest of West-Central Africa from Ivory Coast to West Cameroons, and extending across the Congo basin and Uganda [10, 11]. Its ethnobotanical uses are well documented [2]. The analysis of aqueous, ethanol and methanol extracts of *P. nitida* revealed the presence of tannins, saponins, flavonoids, terpenoids, steroids and glycosides, reducing sugars, carbohydrates and like alkaloids including indole alkaloids; akuammine, pseudoakuammine, akuammidine, akuammicine, akuammigine, pseudoakuammigine, akuammiline and akuammenine [12-16]. Erharuyi and Falodun [2] reported that alkaloids are the major class of phytochemicals isolated from *P. nitida*. They demonstrated that extracts from this plant possess various biological activities including antimalarial, antileishmanial, trypanocidal, larvicidal, antipyretic, analgesic, anticoagulant, anti-inflammatory, anti-diarrhoeal, hypoglycaemic and antimicrobial properties [2]. COVID-19 involves serious complications such as heart injury, with cardiac dysfunction in COVID-19 patients, though its mechanism is still unclear [2]. The valuable properties of the *P. nitida* medicinal plant (including anti-platelet aggregation and anti-lung injury,) make it one the best fits and therefore a potential candidate in the fight against COVID-19. Particularly, the fact that *P. nitida* displays antimalarial activity can help to anticipate that it would show some potency or activity against Covid-19 virus. Indeed, Chloroquine, an antimalarial based-drug which has been synthesized from the alkaloid quinine, has revealed antiCOVID-19 properties [17-19]. Besides, SARS-COV-2 (Covid-19 virus) is an obligate endocytic parasite that behaves both like HIV by attacking T-cells [20] and like Plasmodium spp by destroying haemoglobin [21]. The potential role of medicinal plants and their secondary metabolites in the inhibition of COVID-19 virus has been largely demonstrated by the molecular docking technique [22]. In this article, we present the data on *Picralima nitida* and its major alkaloids that could justify their use in the treatment of COVID-19 in the Democratic Republic of Congo. In addition, the objective of the current study is to review the literature on the nutritional value, phytochemistry and pharmacological properties of *P. nitida*. This data would allow the use of this plant as a multifunctional and low toxicity drug candidate for the management of various diseases, including the COVID-19.

**Methodology**

In this study, we conducted a search of relevant literature of the traditional plant species used as medicines from 1976 to 2020. The plant databases including Sciencedirect, PubMed, Google Scholar and Scopus, were used to retrieve the articles on *Picralima nitida*. The scientific name of this plant species was used as the keyword for the search, along with the terms phytochemistry, bioactivities, pharmacology and pharmacognosy. The chemical structures isolates from this plant naturally occurring compounds were drawn using ChemBioDraw Ultra 12.0 software package. Finally, bibliographical references were made using bibliographical software "Mendeley".

**Botanical description**

*Picralima nitida* Durand and Hook, (fam. Apocynaceae) is the only species of the genus Picralima [2]. When fully grown, the tree has a height up to 15-30 m. Its girth is about 60 cm or more with a dense crown and dark-brown or blackish brown color. The leaves are opposite and simple with stipules. The bark of this plant is hard, brittle, and pale to dark greyish black or brown and smooth to slightly rough or finely striped [12]. The corolla is about 2-5 cm long, glabrous outside with ribbed tube. The calyx is leathery and lobed, keeled shaped and about 2-5 cm long. The ovary is superior. The flowers of this species are bisexual and the fruits occur usually in pairs hanging at the end of a long stalk. It is smooth and has a round apex. It is about 11-20 cm long and 8-10 cm in diameter [23]. The fruit is glabrous and leafy green when unripe but yellow to orange in color when ripened. It has latex and no rubber in the pericarp [12, 23]. Its seeds are embedded in the white soft pulp and are obliquely ovate, obovate to oblong, flattened 2.5-4.5 cm long. These seeds are brown in color and are dicotyledonous with or without coma, endosperm is thick and often hairy, scanty.
Table 1. The alkaloids isolates from different parts of *P.nitida* [25, 28]

| Plant part examined | Alkaloids identified | Mode of action | Plant part examined | Alkaloids identified | Mode of action |
|---------------------|----------------------|----------------|---------------------|----------------------|----------------|
| Root bark           | Picracine            |                | Mature seeds        | akuammicine         | It interacts with opioid receptors |
|                     | Akuammigine          | It reduces hypertension and renal adrenal vasoconstriction |                     | akuammigine         | It Reduces hypertension and renal adrenal vasoconstriction |
|                     | Akuammicine          | It interacts with opioid receptors |                     | pseudo-akuammigine  | It stimulates the central nervous system, respiration, skeletal muscle contraction and smooth muscle contraction, while at high doses it inhibits them |
| Stem bark           | Akuammicine          |                  | Immature seeds      | akuammidine         | This compound reverses the hypertensive action and suppresses the renal vasoconstrictor effects of medium doses of adrenaline; It increases the hypotension caused by the initial doses of N-Ethyl-Norepinephrine and reverses the hypertensive action of medium doses of this amine. |
|                     | Picratidine          |                  |                     | akuammidine         | It increases the sensitivity of the Sympathetic Nervous System to its natural and artificial stimuli. |
|                     | Picracine            | It increases the sensitivity of the Sympathetic Nervous System to its natural and artificial stimuli. |                     | akuammidine         | It Reduces hypertension and renal adrenal vasoconstriction |
|                     | Akuammidine          | This compound reverses the hypertensive action and suppresses the renal vasoconstrictor effects of medium doses of adrenaline; It increases the hypotension caused by the initial doses of N-Ethyl-Norepinephrine and reverses the hypertensive action of medium doses of this amine. |                     | akuammigine         | It Reduces hypertension and renal adrenal vasoconstriction |
| Fruit pods          | Akuammigine          | It reduces hypertension and renal adrenal vasoconstriction. |                     | picraline            | It interacts with opioid receptors |
|                     | Pseudo-akuammigine   | It stimulates the central nervous system, respiration, skeletal muscle contraction and smooth muscle contraction, while at high doses it inhibits them. |                     | akuammigine         | It increases the sensitivity of the Sympathetic Nervous System to its natural and artificial stimuli. |
|                     | Akuammicine          |                |                     | Pseudo-akuammigine  | It stimulates the central nervous system, respiration, skeletal muscle contraction and smooth muscle contraction, while at high doses it inhibits them. |
|                     | Akuammigine          | It reduces hypertension and renal adrenal vasoconstriction |                     | picraline            | It interacts with opioid receptors |
|                     | Picratidine          |                |                     | Pseudo-akuammigine  | It stimulates the central nervous system, respiration, skeletal muscle contraction and smooth muscle contraction, while at high doses it inhibits them. |
The seed has a light brown color, obovoid in shape, and smooth texture [12].

**Microscopy features**

Osuala et al., [12] reported that microscopy of the powdered seeds revealed the presence of sclereids, parenchyma and epidermal cells, calcium oxalate crystal, and fat globules.

**Chemical composition of P. Nitida**

Some researchers have reported several known compounds and secondary metabolites. Phytochemical screening of *P. nitida* has revealed the presence of almost the same phytochemical groups like alkaloids, phenols, tannins, saponins, flavonoids, terpenoids, steroids and glycosides, oxalates, phytates, reducing sugars, carbohydrates, fats and oils in all parts of plant [12-16]. Erharuyi and Falodun [2] reported that alkaloids are the major class of phytochemicals isolated from *P. nitida*. The first set of alkaloids isolated from *P. nitida* are the indole alkaloids [24]. The names of these compounds were obtained from the indigenous name of the plant in Ghana ‘Akuamma’. After these, several alkaloids have been isolated from this plant. Picraphylline, picracine, picraline, picralicine, picratidine, picranitine, burnamine, pericalline and pericine are some of the isolated alkaloids [25, 26]. In another study on *P. nitida*, ten different phytochemical compounds have been characterized, including 2,6-bis (1,1-dimethylethyl)-4-methyl phenol, N1-(4-fluorobenzylideno)-N2-(4-quinolinyl-1-oxide) hydrazine, sulfuric acid butyl cyclohexylmethyl ester, 1,2,3,5-cyclohexanetetrol, alpha-methyl mannofuranoside, hexadecanoic acid, methyl ester, 7-octadecenoic acid, methyl ester, 3,7,11,15-tetramethyl-2-hexadecen-1-ol, N,N-dimethylidodecanamide and N,N-dimethyl decanamide [26].

**Nutrient composition of P. nitida**

The seeds contain vital essential amino acids such as leucine, phenylalanine, tyrosine, and non-essential amino acids.

| Parameter       | Concentration | % Composition |
|-----------------|---------------|---------------|
| Calcium         | 12.686 ppm    | 0.578±0.68    |
| Magnesium       | 11.665 ppm    | 0.359±0.18    |
| Potassium       | 42.537 ppm    | 0.846±0.30    |
| Chlorine        | 159 mg/L      | -             |
| Sodium          | -             | 10.67±0.34    |
| Phosphorus      | -             | 0.367±0.10    |
| Iron            | -             | 172.40±0.70   |
| Zinc            | -             | 55.40±0.30    |
| Manganese       | -             | 38.20±0.20    |
| Selenium        | -             | 0.007±0.10    |

Values are means ± standard deviation of three determinations

| Nutrient composition | Mean composition |
|----------------------|------------------|
| Moisture             | 10.67 ± 0.34     |
| Ash                  | 3.67 ± 0.34      |
| Protein              | 3.50 ± 0.18      |
| Crude fibre          | 8.78 ± 0.68      |
| Fat                  | 3.49 ± 0.10      |
| Total Carbohydrate   | 69.9 ± 0.78      |

Values are means ± standard deviation of three determinations.
The ground seeds contain more unsaturated fatty acids than saturated fatty acids and possess considerable amount of macro and micro-elements with iron, zinc, and manganese. The ground seeds also have vitamins A and E [29]. The results of the proximate composition of this species indicated that P. nitida peels contains an appreciable amount of nutrients: lipid, protein, and carbohydrate as well as moisture and ash [14]. Another study on mineral analysis revealed that the plant contains metals such as Ca++, Mg++, and K+ ions and non-metals, such as Cl- ions[12].

**Pharmacological activities**

**Anticancer activity**
The anticancer activity of *P. nitida* root bark against human epithelial MCF-7 cells has been reported by Engel et al., [45]. Studies have confirmed the presence of alkaloids, tannins, polyphenols, and steroids in *P. nitida*, and these components are associated with the anticancer property of this species.

**Free radical scavenging activities**
The in vitro antioxidant evaluation of methanol extract of *P. nitida* and its fractions using the DPPH free radical scavenging method showed that its crude extract has IC-50 value of 5μg/mL for radical scavenging activity which is significantly higher than that of ascorbic acid (2.55μg/mL). *Picralima nitida* has the potential for use as a natural plant antioxidant in preventing the free radical damage [2]. In another study on determining the antioxidant capacity of ethanol, ether, ethyl acetate, butanol, and aqueous extracts of plant seeds using free radical, it was noted that *P. nitida* seed extract exhibits highest antioxidant capacity [40].

**Antimalarial activity**
The in vitro antimalarial activity of *P. nitida* extracts has been investigated. Iwu et al., [23] indicated that the alkaloid extracts of the fruits of this species exhibit activity against drug-resistant and drug-sensitive malarial strains of *Plasmodium falciparum* and these alkaloids show significant inhibitory activity against both clones of *P. falciparum* at IC50 values of 0.0.1-0.09 g/ml. In another study, the significant inhibitory activity of the methanol fruit extract was obtained on multi-drug resistant human *Plasmodium falciparum* with IC50 value of 1.75 μg/mL [30]. Extracts of different parts (seed, fruit rind, and stem bark) of *P. nitida* showed remarkable inhibitory activity against drug resistant clones of *P. falciparum* at doses of 1.23- 32 μg/mL [46]. The results in vitro antiplasmodial activity of the ethanol seed extract of the plant in chloroquine-sensitive *Plasmodium berghei* infected mice showed that the ethanol seed extract of this plant exhibited a significant in vivo antiplasmodial activity in both early (4-Day chemo-suppressive test) and established infections (Curative test). Ethanolic seed extract of *P. nitida* produced a dose-dependent chemo-suppressive effect of 65.5%, 70.4% and 73.0% respectively for 35, 70 and 115 mg/kg/day doses [31]. Methanol seed extract of *P. nitida* demonstrated significant activity against the chloroquine-resistant *Plasmodium falciparum* W2 strain with IC50 value of (10.9, 1.1) μg/mL [33]. The root, stem bark and fruit rind extracts displayed significant inhibitory activities against the asexual erythrocytic form of *Plasmodium falciparum* with IC50 values of 0.188, 0.545, and 1.581 μg/mL respectively [32].

**Uterotonic effects**
Uterotonic effect of aqueous ethanolic fruit extract of *P. nitida* on uterine contractility was investigated using the rat model [41]. The results of this study revealed that the extract was found to induce a dose-dependent myometrial contraction at concentrations ranging from 0.035- 0.28 mg/ml, whereas concentrations above this range caused a progressive relaxative effect on the uterine muscle tissue. The effective concentrations (EC50) were 0.056 mg/ml and 1.06 mg/ml for contractile and the relaxative responses respectively. These results demonstrated that the extract did not elicit any contractile response in a physiological salt solution devoid of calcium ions. The contractile response
Table 4. The percentage amino acid composition of *P. nitida* seeds [29]

| Amino acids abbreviations | Value (%) | Amino acids abbreviations | Value (%) |
|---------------------------|-----------|---------------------------|-----------|
| Essential Amino Acids     |           | Non-Essential             |           |
| Arginine (Arg)            | 1.25      | Alanine (Ala)             | 0.64      |
| Histidine (His)           | 4.15      | Cysteine (Cys)            | 3.92      |
| Leucine (Leu)             | 11.83     | Glycine (Gly)             | 0.69      |
| Lysine (Lys)              | 3.24      | Proline (Pro)             | 0.81      |
| Methionine (Met)          | 1.64      | Tyrosine (Tyr)            | 6.08      |
| Phenylalanine (Phe)       | 9.21      | Serine (Ser)              | 1.11      |
| Threonine (Thr)           | 0.75      | Glutamate (Gln)           | 2.36      |
| Tryptophan (Try)          | 9.93      | Aspartate (Asp)           | 1.14      |
| Isoleucine (Ile)          | 5.44      | Total NEAA                | 16.75     |
| Valine (Val)              | 9.76      | % Non-Essential           | 25        |
| Total EEA                 | 48.2      | % Essential               | 74%       |

Where: EEA, Essential amino acids; NEAA, Non-essential amino acids, TNEAA, Total Non-essential amino acids

Table 5. The percentage fatty acid composition of *P. nitida* seeds [29]

| Fatty acids | % composition | Unsaturated fatty acids | % composition |
|-------------|---------------|-------------------------|---------------|
| 8.0 Caprylic acid | 1.41          | 16.1 Palmitoleic acid   | 12.05         |
| 10.0 Capric acid  | 1.24          | 18.1 Oleic acid         | 37.85         |
| 12.0 Lauric acid  | 1.95          | 18.2 Linoleic acid      | 40.75         |
| 14.0 Myristic acid | 0.83          | 18.3 Linolenic acid     | 2.75          |
| 16.0 Palmitic acid | 12.05         | 20.3 Arachniodic acid   | 2.02          |
| 17.0 Margaric acid | 1.07          | 21.1 Erucic acid        | 0.09          |
| 18.0 Steric acid   | 5.36          | Total                   | 95.51         |
| 22.0 Behenic acid  | 0.05          | % Unsaturated fatty acids | 78.87%       |
| 24.0 Lignoceric acid | 0.11          |                         |               |
| Total Saturated fatty acids | 24.07       |                         |               |
| % Saturated fatty acids | 20.13%       |                         |               |
| Total fatty acids    | 119.58       |                         |               |

evoked by a fixed concentration of the extract (0.07 mg/ml) decreased as the concentration of verapamil (0.02-0.2 µmol) increased. The extract (0.07 mg/ml) did not restore the spontaneous myometrial contraction previously abolished by adrenaline (9.1 nmol) and a selective β-adrenergic receptor agonist, salbutamol (0.2 µmol) respectively. However, about 26.3% contraction was observed when a non-selective β-adrenergic stimulant, isoprenaline (0.1 µmol) was added simultaneously with the extract. Also, propranolol (0.3 µmol) potentiated the contractile response of this extract.
Antipyretic and analgesic activities
Ezeamuzie et al., [30] demonstrated the antipyretic activity of methanol fruit extract of *P. nitida*. The result of the present study revealed that the methanol fruit extract at a dose of 50 mg/kg produced a mean percentage antipyrexia of 38.7% on lipopolysaccharide induced pyrexia in rabbits, which was comparable to aspirin (29.0% at 200 mg/kg). Extracts of the plant have been shown to possess significant analgesic activity in the rat pedal model [23].

Antidiabetic activity
Teugwa et al., [39] reported that the hydroethanolic extract of whole plants (150 mg/Kg) and methanol leave extract of the plant (300 mg/Kg) exhibited significant antidiabetic activities with 39.40% and 38.48% glycemia reduction, respectively. Inya-Agha et al., [47] investigated the hypoglycemic effect of the methanol extracts of seed, and fruit rind of *P. nitida* in rats. The result of this study showed a significant (P<0.01) hypoglycemic effect of all extracts at 300 and 900 mg/kg in alloxan-induced diabetes in rats. In another study, Aguwa et al., [48] confirmed the hypoglycemic effect of the aqueous seed extract of *P. nitida* in alloxan-induced diabetic rabbits.

Microbial activities
Studies on *P. nitida* indicate that extracts from this plant have an action against *Staphylococcus aureus, Enterococcus faecalis, Bacillus cereus, Escherichia coli, Salmonella typhi*, and *Proteus mirabilis* [14, 27]. These results give credence to the use of the extract in herbal medicines for the treatment of
Table 6. The extract, concentration, standard, model system used, pharmacological action and plant part biologically active compounds isolated from P. nitida

| Plant parts                  | Extract                | IC50 or CMI           | Standard               | System model           | Biological activities                          | Reference |
|------------------------------|------------------------|-----------------------|------------------------|------------------------|-----------------------------------------------|-----------|
| Fruits                       | Methanol extract       | 1.75 µg/mL (10.9±1.1) µg/mL | Chloroquine and Quinine | Plasmodium falciparium | Antimalarial activity                         | [23, 30-33] |
| Seeds                        | Ethanol extract        | 35, 70 and 115 mg/kg/day doses | -                      | Plasmodium falciparium |                                |           |
| Seeds, fruit rind, stem bark | Alkaloids extract      | 0.61-09 g/mL          | -                      |                        |                                |           |
| Root, stem bark              |                        |                       |                        |                        |                                |           |
| and fruit rind extracts      | -                      | 0.188, 0.545 and 1.581 µg/mL |                        |                        |                                |           |
| Seeds                        | Chloroform extract     | -                     | Leishmania donovani     |                        | Antileishmanial activity                      | [34]      |
| bark                         | Water extract          | 8 mg/kg               | -                      | Mice                   |                                |           |
| Leaf                         | Ethanolic and aqueous extracts | 0.660% and 1.057% w/v |                        |                        |                                |           |
| Leaf and seed                | Aqueous, methanol      | 0.164, 0.333 and 0.150 mg/mL | -                      |                        |                                |           |
| Seeds                        | Ethanol extract        | P<0.05                | -                      | Guinea pig brain, Rats | Analgesic activity                       | [26, 30] |
| Fruits                       | Methanol extract       | 50mg/kg               | Aspin                  | Rabbits               | Antipyretic activity                      | [30]      |
|                           |                        | 5.0 mg/kg; 102 mg/kg | -                      | Rats                   | Anti-inflammatory activity                 | [37]      |
|                           |                        |                       |                        |                        |                                |           |
| Stem bark and leaves and seeds | methanol and hydroethanol extracts | 300 mg/kg          | Insulin                | Mice                   | Antidiabetic activity                     | [39, 40] |
| seed, stem bark and root     | Ethanol, benzene,      | -                     | E. coli, P. aeruginosa, B. subtilis, S. aureus, S. hinthambo | | Antimicrobial activity                  | [38, 39] |
|                             | chloroform and         | -                     |                        |                        |                                |           |
|                             | aqueous (cold and hot) | extracts              |                        |                        |                                |           |
|                   | methanol, Pet-Ether,    | 5μg/mL                | ascorbic acid          | Blood cells            | Free Radical Scavenging Activities         | [2, 40]  |
|                   | Chloroform, Ethyl acetate fraction |                     |                        |                        |                                |           |
| Fruit                       | Ethanolic extract      | 0.056 mg/ml and 1.06 mg/ml | -                      | Rats                   | Uterotonic effects                      | [41]      |
| Seeds                       | Methanol extract       | 10mg/kg               | Aspin                  | Wistar rats            | Hepatotoxicity                          | [42]      |
|                           | Methanol extract and   | 1000mg/kg             | -                      | Rats                   | Anti-ulcer activity                  | [43]      |
|                           | chloroform fraction    |                       |                        |                        |                                |           |
|                           | Aqueous decoction      | 3000 mg/kg/p.c./ou    | -                      | Mouse                  | Acute toxicity                          | [44]      |
| Whole plant and leaf        | Hydroethanol and methanol extract | 150mg/kg            | -                      |                        | Antidiabetic activity                  | [39]      |

diseases and infections. Ubulom et al., [15] reported that both the aqueous and ethanol leaf extracts of P. nitida exerted an antifungal effect on Aspergillus flavus and C. albicans in a dose-dependent manner, but no antifungal effect was exhibited against Microsporum canis. The basic fraction of the methanol extract of the stem bark of this species has been shown to exhibit significant antimicrobial activity against a wide range of Gram-positive bacteria and fungi, but limited activity against Gram-negative bacteria [49].
**Anti-leishmanial activity**
The chloroform extract of the seed of *P. nitida* was evaluated for possible antileishmanial activity using a radiorespirometric micro-test technique and the result of this study confirmed its activity against *Leishmania donovani* at 50 µg/mL [34].

**Antiulcer activity**
Okonta et al., [43] demonstrated the antiulcer activity of *P. nitida* extracts. In this study, oral administration of the methanol extract, chloroform fraction and methanol fraction at 1000 mg/kg reduced gastric ulcer by 56.4%, 40.0%, and 56.3%, respectively; and the fractions of the extract significantly (P<0.05) reduced gastric emptying time when compared to the control. Gastric acidity was significantly decreased when compared with saline group, 40.25 mEq/L in methanol extract, 50.0 mEq/L in methanol fraction but had no significant effect on gastric secretion volume.

**Hepatoprotective activity**
Results of Idu et al., [42] showed that the treatment with *P. nitida* extracts had no adverse effect on the body weight of Wistar rats. Biochemical analysis showed increase in CAT and GSH which are good antioxidant agents. Photomicrographs show moderate amelioration from steatosis caused by Carbon tetrachloride in the treatment groups.

**Toxicopathological and acute toxicity**
Taofik et al., [50] reported that the extract had no significant effect on all kidney function indices assayed but caused a significant reduction (P < 0.05) in the activities of liver enzymes accompanied by a significant decrease in the liver to body weight ratio, serum total protein, and globulin concentrations. No significant alteration was observed in the serum levels of albumin and conjugated bilirubin, whereas the extract brought about a significant increase (P < 0.05) in serum total bilirubin concentration. In this study, the hematomorphological analysis revealed no significant effect on erythrocyte indices in contrast to white blood cell count and its differentials which were significantly elevated (P < 0.05) following the extract administration. The acute toxicity of seeds aqueous decoction from *P. nitida* was assessed after giving the crude decoction to mice in increasing doses ranging from 600 to 3000 mg/kg of body weight (b.w.). The use of the herbal medicine, through oral route (or), at different doses, does not cause some clinical signs. The results made it possible to obtain the dose at bordering on solubility which squares with the tolerated maximal dose or TMD (3000 mg/kg/b.w./or). This toxicological parameter (tolerated maximal dose) is by far higher than 94.885 mg/kg b.w./or, the recommended daily dose by traditional healers. Therefore, the dose prescribed by traditional healers is not toxic, justifying the use of the plant in traditional conditions of preparation and oral administration.

**Conclusion and future prospects**
The Covid-19 pandemic is a major health crisis of the 21st century for which no cure is currently available and which requires an alternative solution based on the endogenous knowledge. *P. nitida* medicinal plant species owing to its valuable properties have been used traditionally in folk medicines to treat various ailments including malaria, which make it the best candidate in the fight against the current dread disease. The current study aimed to review the literature on the traditional use, nutritional value, phytochemistry, and biological properties of this valuable plant species. The results of the bibliographic investigation showed that *P. nitida* treats several diseases including diabetes mellitus and malaria, etc. Concerning the phytochemistry, several compounds have been identified including several alkaloids, as the major class of compounds of these species whose properties make this plant a potential anti-COVID-19 candidate. Molecular docking studies are,
therefore, necessary to evaluate the binding reaction of alkaloids with the major SARS-COV-2 target enzymes.

Acknowledgements

The authors highly acknowledge the contributions of different researchers included in the text as references. Both departments of Biology and Chemistry, University of Kinshasa, Kinshasa, Democratic Republic of the Congo, the Research Focus Area for Chemical Resource Beneficiation (CRB), Catalysis and Synthesis Research Group, North-West University, Potchefstroom, South Africa, and the Department of Environmental Sciences, University of Gbadolite, Nord-Ubangi, Democratic Republic of the Congo are herein acknowledged.

References

[1] P. T. Mpiana, K. N. Ngbolua, D. S. T. Tshibangu, J. T. Kilembe, B. Z. Gbolo, D. T. Mwanangombo and C. L. Inkoto et al., (2020). Aloe vera (L.) Burm. F. as a potential anti-COVID-19 plant: a mini-review of its antiviral activity. European J. Med. Plants, 31: 86-93.

[2] O. Erharuyi and A. Falodun (2012). Free radical scavenging activities of methanol extract and fractions of Picralima nitida (Apoecanacea). J. Appl. Sci. Environ. Manage., 16: 291-294.

[3] R. P. Borris (1996). Natural Product Research: Perspectives from a major pharmaceutical company. J. Ethnopharmacol., (51): 29-38.

[4] G. N. Anyasor, D. A. Aina, M. Olushola and A. F. Aniyikaye (2011). Phytochemical constituent, proximate analysis, antioxidant, antibacterial and wound healing properties of leaf extracts of Chromolaema Odorata. Ann. Biol. Res., 2: 441-451.

[5] H. L. Nkasa, C. L. Inkoto, J-C. M. Muzomwe, E. I. Masengo, C. M. Muzomwe, C. M. Mulenga and K. M. Taba (2020). Phytochemical screening and antibacterial activity of phytomedicine mathesia, a drug use against buruli ulcer in republic democratic of the congo (drc). Eur. J. Pharm. Med. Res., 7: 52-56.

[6] C. L. Inkoto, G. N. Bongo, P. M. Kapepula, C. A. Masengo, B. Z. Gbolo, C. Tshiama and N. K. Ngombe (2017). Microscopic and phytochemical assays of selected congolese medicinal plants: Aframomum alboviolaceum (Ridley) K. Schum, Annona senegalensis Pers. and Mondia whitei (Hook.f.) Skeels. Emer. Life Sci. Res., 3: 1-10.

[7] E. N. Ipona, C. L. Inkoto, G. N. Bongo, C. M. Mulenga, B. L. Ilunga, O. S. Shetonde and B. M. Mbala (2019). Ethno-botanical survey and ecological study of medicinal plants traditionally used against erectile dysfunction in Democratic Republic of the Congo; Bioscience and Bioeng., 4: 85-91.

[8] J. B. Iteku, O. Mbayi, G. N. Bongo, P. K. Mutwale, J. M. Wambale, E. Lengbiye and C. L. Inkoto (2019). Phytochemical analysis and assessment of antibacterial and antioxidant activities of Phytolacca dodecandra L. herit leaf extracts (Phytolaccaceae). Int. J. Biomedical Engineering Clinical Sci., 5: 31-39.

[9] D. D. Tshilanda, C. L. Inkoto, K. Mpongou, Z. Mata, P. M. Kapepula, D. S.-T. Tshibangu and G. N. Bongo et al., (2019). Microscopic Studies, Phytochemical and Biological Screenings of Ocimum canum. Int. J. Pharmacy Chem., 5: 61-67.

[10] J. E. Ajanohoun, N. Aboubakar, K. Diamante, M. E. Ebot, J. A. Ekpere and E. G. Enow-Orock et al., (1996). Contribution to ethnobotanical and floristic studies in Cameroun. Traditional medicine and Pharmacopoeia. Technical and Research Commission of the Organisation of African Unity. OAU/STRC; 1996, 60-61.

[11] T. F. Okujagu, S. O. Etatuvie, I. Eze, B. limoh, C. Nwokereke, C. Mbaoji, and Z. Mohammed (2008). Medicinal plants of Nigeria; South East Zone, Vol. 1." Lisida Consulting, Lagos.
[12] F. N. Osualaa, S. I. Inya-Agha, U. E. Odoh, C. O. Ezeugwu and S. C. Ohadoma (2018). Pharmacognostic studies on the seeds of *Picralima Nitida* Stapf (Apocynaceae). Int. J. Pharmacy, 548-563.

[13] L. B. K. Mabeku, J. Kouam, A. Paul and F. X. Etoa (2008). Phytochemical screening and toxicological profile of methanolic extract of *Picralima nitida* fruit rind (Apocynaceae). Toxicol Environ Chem, 90: 815-828.

[14] N. A. Obasi, U. C. Okorie, B. N. Enemchukwu and G. Otuchristian (2012). Nutritional evaluation, phytochemical screening and antimicrobial effects of aqueous extract of *Picralima nitida* peel. Asian J. Biol. Sci., 5: 105-112.

[15] M. P. E. Ubolom, N. G. Imandeh, C. E. Udobi and I. Ilia (2012). Larvicidal and antifungal properties of *Picralima nitida* (Apocynaceae) leaf extracts. Eur. J. Med. Plants, 2: 132-139.

[16] L. B. M. Koutcheu, J. L. Tamesse and J. Kouam (2013). The anti-shigellosis activity of the methanol extract of *Picralima nitida* on Shigella dysenteriae type I induced diarrhoea in rats. BMC Compl Altern Med., 13: 211. doi: 10.1186/1472-6882-13-211

[17] A. Cortegiani, G. Ingoglia, M. Ippolito, A. Giarratano and S. Einav (2020). A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. J. Crit. Care, 57: 279-283.

[18] T. Y. Hu, M. Frieman and J. Wolfram (2020). Insights from nanomedicine into chloroquine efficacy against COVID-19. Nat. Nanotechnol., 15: 247-249.

[19] P. Gautret, J.-C. Lagier, P. Parola, V. T. Hoang, L. Meddeb, M. Mailhe and B. Doudier et al., (2020). Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int. J. Antimicrob. Agents, doi: 10.1016/j.ijantimicag.2020.105949.

[20] W. Xinling, X. Wei, H. Gaowei, X. Shuai, S. Zhiping, L. Zezhong and X. Youhua et al., (2020). SARS-CoV-2 infects T lymphocytes through its spike protein-mediated membrane fusion. Cell. Mol. Immunol., doi: 10.1038/s41423-020-0424-9

[21] L. Wenzhong and L. Hualan (2020). COVID-19: attacks the 1-beta chain of hemoglobin and captures the porphyrin to inhibit human heme metabolism. ChemRxiv. Preprint. doi: 10.26434/chemrxiv.11938173.v8.

[22] K. Jiti, K. Hendra, K. Rizki, S. Suhartati and S. Soetjipto (2020). Potential inhibitor of Covid-19 main protease (Mpro) from several medicinal plant compounds by molecular docking study. Preprints; 2020030226. doi: 10.20944/preprints202003.0226.v1.

[23] M. M. Iwu (1993). Handbook or African medicinal plants, CRC press, London, Boca Raton, FL, 183-184.

[24] T. A. Henry and T. M. Sharp (1927). CCLIV.—The alkaloids of Picralima Klaineana. Journal of the Chemical Society (Resumed), 1950-1959.

[25] P. Tane, M. Tene and O. Sterner (2002). Picranitine, a new indole alkaloid from *Picralima nitida* (apocynaceae). Bull. Chem. Soc. Ethiop., 16: 165-168.

[26] J. R. Menzies, S. J. Paterson, M. Duwiejua and A. D. Corbett (1998). Opioid activity of alkaloids extracted from *Picralima nitida* (fam. Apocynaceae). Eur. J. Pharmacol., 350: 101-108.

[27] U.I. Ukenwa and N.M. Mary-Ann (2014). Chemical profiling and antibacterial activity screening of the leaves of *Picralima nitida* (apocynaceae). Int. J. Medicinal Chemistry and Analysis, 4: 155-161.

[28] B.L. Moller, Seedorff and F. Nartey (1972). Alkaloids of *Picralima nitida*. Phytochemistry, 2620-2621.

[29] A. N. Linus (2016). Chemical profile of *Picralima nitida* Seeds used in ethnomedicine in West Africa. FUTOJNLS, 2: 110-122.

[30] I. C. Ezeamuzie, M. C. Ojinnaka, E. O. Uzogara and S. E. Oji (1994). Anti-inflammatory, antipyretic and anti-malarial activities of a West African medicinal plant- *Picralima nitida*. Afri. J. Medicine Med. Sci., 23: 85-90.
[31] J. E. Okokon, B. S. Antia, A. C. Igboasoiyi, E. E. Essien and H. O. C. Mbagwua (2007). Evaluation of antiplasmodial activity of ethanolic seed extract of Picralima nitida. J Ethnopharmacol., 111: 464-467.

[32] G. François, L.A. Assi, J. Holenz and G. Bringmann (1996). Constituents of Picralima nitida display pronounced inhibitory activities against asexual erythrocytic forms of Plasmodium falciparum in vitro. J. Ethnopharmacol., 54: 113-117.

[33] J. Bickii, G.R.F. Tchouya, J.C. Tchouankeu and E. Tsamo (2007). Antimalarial activity in crude extracts of some Cameroonian medicinal plants. Afr J Trad. CAM., 4: 107-111.

[34] M. M. Iwu, J. E. Jackson, J. D. Tally and D. L. Klayman (1992). Evaluation of plant extracts for antileishmanial activity using a mechanism-based radiospirometric microtechnique (RAM). Planta Medica, 58: 436-441.

[35] L. O. Wosu and C. C. Ibe (1989). Use of extracts of Picralima nitida bark in the treatment of experimental trypanosomiasis: A preliminary study. J Ethnopharmacol, 25: 263-268.

[36] U. M. E. Dibua, G. E. Odo, O. F. Nwabor and G. I. Ngwu (2013). Larvicidal activity of Picralima nitida, an environmental approach in malaria vector control. Am. J. Res. Comm., 40: 2325-2336.

[37] M. Duwiejua, E. Woode and D. D. Obiri (2002). Pseudo-akuammigine, an alkaloid from Picralima nitida seeds, has anti-inflammatory and analgesic actions in rats. J. Ethnopharmacol., 81: 73-79.

[38] C. V. Iroegbu and C. K. Nkere (2005). Evaluation of the antibacterial properties of Picralima nitida stem bark Extracts. Int. J. Mol. Med. Adv. Sci., 1: 182-189.

[39] C. M. Teugwa, P. C. Mejiato, D. Zofou, B. T. Tchinda and F. F. Boyom (2013). Antioxidant and antidiabetic profiles of two African medicinal plants: Picralima nitida (Apocynaceae) and Sonchus oleraceus (Asteraceae). BMC Compl. Altern. M., 13: 175.

[40] H. Shittu, A. Gray, B. Furman and L. Young (2010). Glucose uptake stimulatory effect of akuammicine from Picralima nitida (Apocynaceae). Phytochem. Lett., 3: 53-55.

[41] C. M. Edmund, S. O. Izuchukwu, O. O. Ebere, E. O. Chiadikobi, C. N. Ernest, A. A. Oluwa and N. U. Chukwuka (2014). In vitro Uterotonic Effects of Ethanolic Fruit Extract of Picralima nitida (Stapf) on isolated uterine smooth muscles of rats. J. Agri. Vet. Sci., 7: 37-43.

[42] I. M. Donald, O.-U. Oghale, E. G. Ikechi and O. A. Orji (2016). Hepatoprotective potentials of Picralima nitida against in vivo carbon tetrachloride-mediated hepatotoxicity. J. Phytopharmacology, 5: 6-9.

[43] J.M. Okonta, M. O. Adibe and C. M. Ubaka (2011). Antiulcer activity of methanolic extract and fractions of Picralima nitida seeds (Apocynaceae) in rats. Asian Pac. J. Trop. Med., 4: 13-15.

[44] N. G. Koffi, A. A. Emma and D. K. Stephane (2014). Evaluation of Picralima nitida acute toxicity in the mouse. Int. J. Res. Pharm. Sci., 4: 18-22.

[45] N. Engel, A. Falodun, J. Kühn, U. Kragl, P. Langer and B. Nebe (2014). Pro-apoptotic and anti-adhesive effects of four African plant extracts on the breast cancer cell line MCF-7. BMC Compl. Altern. M., 14: 334.

[46] M. M. Iwu and D.L. Klayman (2002). Evaluation of the in vitro antimalarial activity of Picralima nitida extracts. J Ethnopharmacol., 36: 133-135.

[47] S. I. Inya-Agha, S. C. Ezea and O. A. Odukoya (2006). Evaluation of Picralima nitida: Hypoglycaemic activity, toxicity and analytical standards. Plant Med., 72: P.025. doi: 10.1055/s-2006-949825.

[48] C. N. Aguwa, C. V. Ukwe, S. I. Inya-Agha and J. M. Okonta (2001). Antidiabetic effect of Picralima nitida aqueous seed extract in experimental rabbit model. J. Nat. Rem., 1: 135-139.

[49] T. O. Fakeye, O.M. Itiola, H. A. Odelola (2000). Evaluation of the antimicrobial property of the stem bark of Picralima nitida (Apocynaceae). Phytother. Res., 14: 368-370.

[50] O. S. Taofik, B. O. Oyelola, A. O. Tajudeen, T. Y. Musa and O. D. Omotayo (2014). Toxicopathological evaluation of Picralima nitida seed aqueous extract in Wistar rats. Turk. J. Biochem., 39: 119-125.