Traditional Methods for Treatment and Management of Measles in Northern Nigeria: Medicinal plants and their molecular docking

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Research

Abstract

Background: Measles is one of the major causes of death among young children worldwide. According to the World Health Organization, measles affects more than 20 million people globally each year, with around 17 millions of them being children. In Nigeria, traditional herbal medicine has long been employed to treat this disease.

Methods: Purposive sampling was used with the aid of an open-ended interview guide, from March–December 2021. In addition, a literature search was carried out on the reported plants. Molecular docking-based virtual screening was employed to identify possible compounds with higher affinity to the target enzyme.

Results: Twenty-four medicinal plants and three traditional methods were documented for the treatment and management of measles in Northern Nigeria. Cow dung and fermented *Sorghum* had the highest Fidelity Level at 100 %, respectively. Leaves were the most common plant part used for the treatment of measles, likely due to the presence of secondary metabolites. Decoction and oral application were the most effective methods of preparation

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and administration, respectively. The binding affinities of the investigated compounds ranged from -1.3 Kcal/mol to -9.3 Kcal/mol, respectively. From the molecular docking, Quinoline and Amyrin were identified to have the highest binding affinity of -9.3 Kcal/mol, respectively.

Conclusion: This study adds to our understanding of the plants utilized by Northern Nigerians in the prevention and treatment of measles. These data may be used to further pharmacological research on these therapeutic plants, with a focus on safety, standardization, and effective dose.

Keywords: African Medicinal Plant, Measles, Medicinal plants, Nigeria, In Silico

Background

Infectious diseases are the leading cause of death in tropical nations, accounting for over half of all human deaths (Musa *et al.*, 2015). This is largely a result of the declining efficacy of common drugs, due to the growth of drug-resistant infections, particularly in underdeveloped nations where poverty and illiteracy are high and basic health services are lacking (Musa *et al.*, 2015). The measles virus is highly contagious, and measles killed an estimated 2.6 million people each year before widespread vaccination in 1980 (Oluremi & Adeniji, 2015). Measles is a major cause of death among young children worldwide, despite the availability of a safe and cost-effective vaccination (Oluremi & Adeniji, 2015; Strebel *et al.*, 2003). Measles is a devastating viral disease that affects the world's most vulnerable children, many of whom lack access to healthcare (Sonibare, Moody & Adesanya, 2009). Fever, cough, conjunctivitis, and broad maculopapular rash are all symptoms (Furuse *et al.*, 2010). According to the World Health Organization, measles affects more than 20 million people worldwide each year, with around 17 millions of them being children (Sonibare *et al.*, 2009, Parker *et al.*, 2007; Dogara *et al.*, 2022). As a result of measles' secondary complications, including pneumonia, encephalitis, and diarrhea, a total of 242,000 patients died, e.g., in 2006 (Control & Prevention, 2007), and in 2013 still over 145,700 people died from measles, the majority of them children under the age of five (Oluremi & Adeniji, 2015). Antiviral drugs that suppress viral replication inside monocytes may be especially useful in reducing illness severity. Therefore far, only high dose vitamin A has been found to have any therapeutic impact in acute measles infection (Parker *et al.*, 2007), and measles still has neither a therapy nor a cure (Sonibare *et al.*, 2009). Plants have always been used by humans in many forms, including in traditional medicine. They contain a wide range of biologically active substances, many of which are therapeutic in nature (A. Dogara *et al.*, 2021; Dogara *et al.*, 2021). The notion of computer-aided drug design (CADD) has widely been adopted to save time and reduce the cost involved in designing or discovering novel small molecules with better potency. Molecular docking virtual screening is widely employed in structure-based drug design (SBDD) and plays a vital role when predicting the binding orientation and affinities of two molecules when bound together to form a stable complex (Ibrahim *et al.*, 2021). Assessment of the binding behavior plays a significant role in the rational design of small molecules as well as explaining the important biochemical processes involved (Ferreira *et al.*, 2015). Molecular docking is a very powerful *in silico* method in the therapeutic industry for finding new treatments for unmet medical wants predicting drug-target interactions, it provides binding affinity between drugs and their target receptors at the atomic level and elucidates the fundamental pharmacological properties of a specific drug (Shadrack *et al.*, 2018). The diverse Nigerian flora might provide interesting compounds that could be used to develop new treatments for the deadly measles virus. One study previously assessed the effect of medicinal plants on the treatment of measles in the western part of Nigeria (Sonibare *et al.*, 2009). The current study aims to explore the medicinal plants of the northern part of Nigeria used for the management and treatment of measles virus, and the application of *in silico* model prediction for possible exploration to formulate herbal products and modern drugs.

Materials and Methods

Study area

An ethnobotanical study was conducted in Kaduna state (10° 35" N, 7° 19" E), Northern Nigeria, which has a population of 6,066,562 people and covers 46,056 km^2. The majority of the population are Hausa and Fulani (nomadic) (Dogara *et al.* 2021). Work as civil servants, farming, animal husbandry, fishing, and hunting are among their main activities. The area is primarily defined by two seasons: dry (October-May) and wet (June-September), although this fluctuates depending on the year (A. Dogara, Hamad, *et al.*, 2021).

Sampling and interview sessions

AS nonrandom probability strategy was used for expert sampling in Kaduna's three geopolitical zones (Figure 1). An open-ended interview was adopted (Abdulrahman, 2021; Kayfi & Abdulrahman, 2021). Experts validated the questionnaire before it was used in the study, and a pilot study was carried out. The data for this study came from direct interviews with traditional herbalists, conducted between March and December 2021. Each respondent was

visited three to four times to ensure that the data was accurate. If there was a discrepancy between the information provided previously and the information received during subsequent trips to a particular plant, it was deemed unreliable and dismissed. Data was obtained using the local language in the area. Of the originally contacted 87 traditional herbalists across the state, only 48 were interviewed after obtaining their prior informed consent.

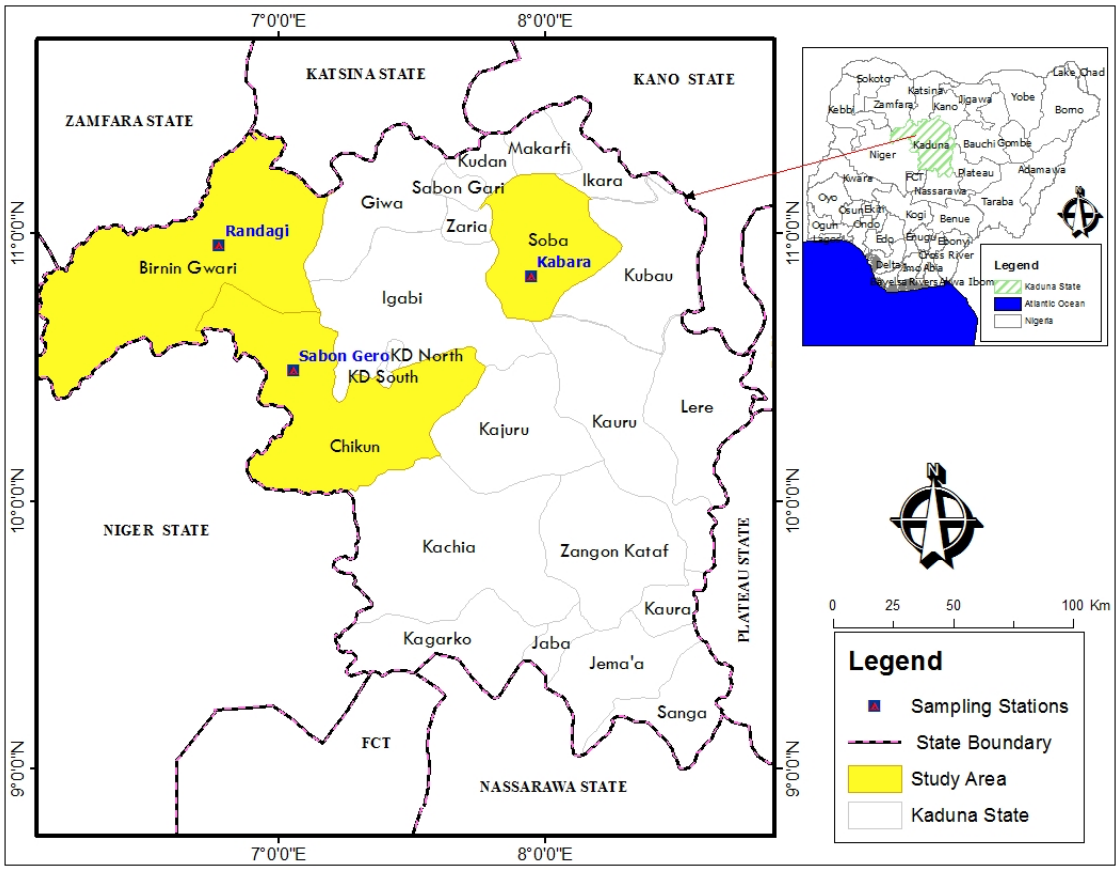

Figure 1. Map of Kaduna state

Plant collection and herbarium deposition

Herbarium specimens were prepared from plant samples taken in the wild and from cultivated gardens. The plants were identified in the field by a trained taxonomist and then cross-checked with herbarium specimens and deposited at Ahmadu Bello University's herbarium in Zaria. A voucher number was assigned (Table 1).

Data analysis

1. Descriptive analysis was computed using Excel 2016. The following Socio-demographic information of the respondents was used to calculate the frequencies and percentages (Abdulrahman *et al.*, 2018; Mahmoud *et al.*, 2020):

I. Gender
II. Educational level
III. Occupational status

2. Using plant taxonomic information, the following frequencies and percentages were also computed:

I. Occurrence of genus
II. Occurrence of families
III. Part of the plant used
IV. Method of administration
V. Method of preparation
VI. Experience

3. The following quantitative ethnobotany indices were applied:

I. **Use Value: UV = Ui / N.,** Where Ui is the total number of users reported by each respondent, and N represents the total number of informants interviewed (Mahmoud & Abba, 2021).

II. **Relative Frequency of Citation (RFC): = Fc/N**, where Fc is the number of people who mentioned a particular plant species and N is the overall number of respondents interviewed (Abdulrahman *et al.*, 2018).

III. **Fidelity level: FL = Ns / N × 100**. Ns = total number of respondents who indicated they employed a specific plant species to treat a specific condition, and N = total number of informants who mentioned the plant species during the interview (Mahmoud, Labaran, & Yunusa, 2020).

Literature search to obtain biological active compounds

Keywords including anti-inflammatory, pain, anti-virus, anti-measles, antimicrobial, antibacterial, chemical composition, phenolic content, flavonoids and other chemical terms were used in a search for each of the reported plants, documenting its activity and the reported major compounds to validate the claimed of the respondents and to run for *in silico* predictions.

Software and computational environment

The nature of interactions between the binding pose of the enzyme receptor and the investigation compounds were investigated using Spartan Pyrex virtual screening software, UCSF Chimera, and Discovery Studio visualizer software, respectively.

Generation of structure, stable conformation calculation and preparation

In this study, the 2D-structures of the investigated compounds were generated using Chemdraw software from University of Cambridge (Mills, 2006). After generation of the structure of the studied molecules, energy minimization was carried out to eliminate constraints in the structures before ascertaining their most stable conformation using density function theory (DFT) at B3LYP/6-311G* level of theory. Ligands were prepared before the docking-based virtual screening analysis by saving the optimized structures in pdb file format (Ibrahim *et al.*, 2020a).

Protein retrieval and preparation

The 3D structure of the enzyme receptor (Measles Virus Nucleoprotein Core in Complex with an N-Terminal Region of Phosphoprotein) with pdb entry code: **5E4V** was retrieved from the RCSB pdb database. The enzyme receptor was prepared by adding polar hydrogen. Then the water molecules and coligand were completely removed from the 3D structure and saved in pdb file format (Abdullahi *et al.*, 2020).

Docking based virtual screening analysis

Blind docking of the investigated compounds to the binding pose of the enzyme receptor was achieved using vina of Pyrex virtual screening software. After a successful docking procedure, the recoupling of the docked investigated compounds and the receptor for further investigation was achieved with UCSF Chimera software (Ibrahim, Uzairu *et al.*, 2020b). Discovery studio was used for the visualization of recoupled complexes to view the mode of interaction (Ibrahim *et al.*, 2019).

Drug-ability/drug-likeness and ADMET properties prediction

The drug-ability/drug likeness and ADMET-pharmacokinetics properties of the investigated compounds were predicted using a free web tool used in evaluating ADMET properties and drug likeness of small molecules (SwissADME (http://www.swissadme.ch/index.php) and pkCSM (http://structure.bioc.cam.ac.uk/pkCSM) (Daina *et al.*, 2017; Ibrahim *et al.*, 2020). In this study, Lipinski's rule of five filters (which states that if any chemical compound violates more than one of these criteria: Molecular weight ≤ 500g/mol, number of hydrogen bond donors ≤ 5, number of hydrogen bond acceptors ≤ 10, calculated logP ≤ 5, the molecule is said to be impermeable or badly absorbed) was used to predict the drug likeness of the investigated compounds.

Results

Socio demographic Information and Schematic life cycle of Measles Virus

A total of 48 respondents were interviewed. Out of these, 39 were men and nine women. Overall, 70.83% of the interviewed respondents had only attended primary education, 22.9% had secondary education, while only 6.25% attended tertiary education. Figure 2 presents the working experience of the interviewed respondents with a dominance of 40 -59 years accounting 58.33%. The route of the infection of measles virus and step taking in the treatment of the virus are presented in Figure 3. The MV infects infants through respiration, rapidly multiply, and got separated all over their body by attacking the immune cells (Figure 3).

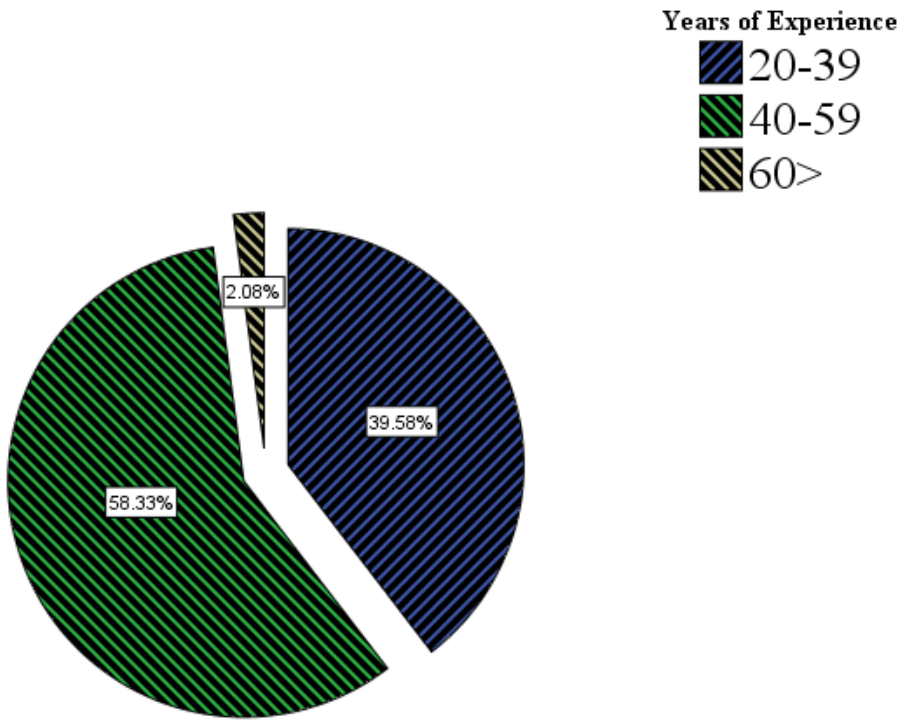

Figure 2. Experience of the respondents in the traditional medicinal systems

Traditional approaches and medicinal plants used for the treatment and management of measles virus
Only plants that were fully authenticated were included in the further analysis of this study. Twenty-four medicinal plants from 24 families and 24 genera (Table 1) were documented as effectively used in the management and treatment of measles diseases in northern Nigeria, and 3 traditional treatment methods were utilized in the region (Table 1). *Solanum lycopersicum* was used for the treatment of rashes on the tongue caused by measles virus. The most popular traditional approach reported was the use of fresh cow dung, however (Table 1).

Part of the plant used, method of preparation and administration
The results indicated that leaves were the most used plant part, followed by the bark and root (Figure 4). Decoctions were used most frequently, followed by infusion and mixing the medicinal plant with oil, honey, or other substances, while mixing with water had the least number of reports (Figure 5). Most preparations included multiple components, and oral application was the most common (Figure 6).

Diagnosis, dosage, number of treated patients, duration of treatment, and toxicity
Measles is known in the region as "*bakon dauru*" "*Bi iska*," or "*kyanda*." Symptoms include an increase in body temperature, diarrhea, headache, body weakness, vomiting, rashes on the tongue, loss of appetite, and constipation. The respondents reported the usage of tea and tablespoons as measuring gauges for the administration of the plant preparations. Some participants reported only a drop should be administered. When the respondents were asked about the number of patients treated, none could provide an exact number. However, all of them reported that cases occurred daily, especially during winter. The respondents reported no specific period for treatment, as normally measles led to other complications that needed to be treated also. Respondents agreed that using plants to treat ailments had no detrimental side effects, according to their expertise. However, some respondents believed that the use of plants could be dangerous if the extracts were taken in big amounts or with the incorrect prescription.

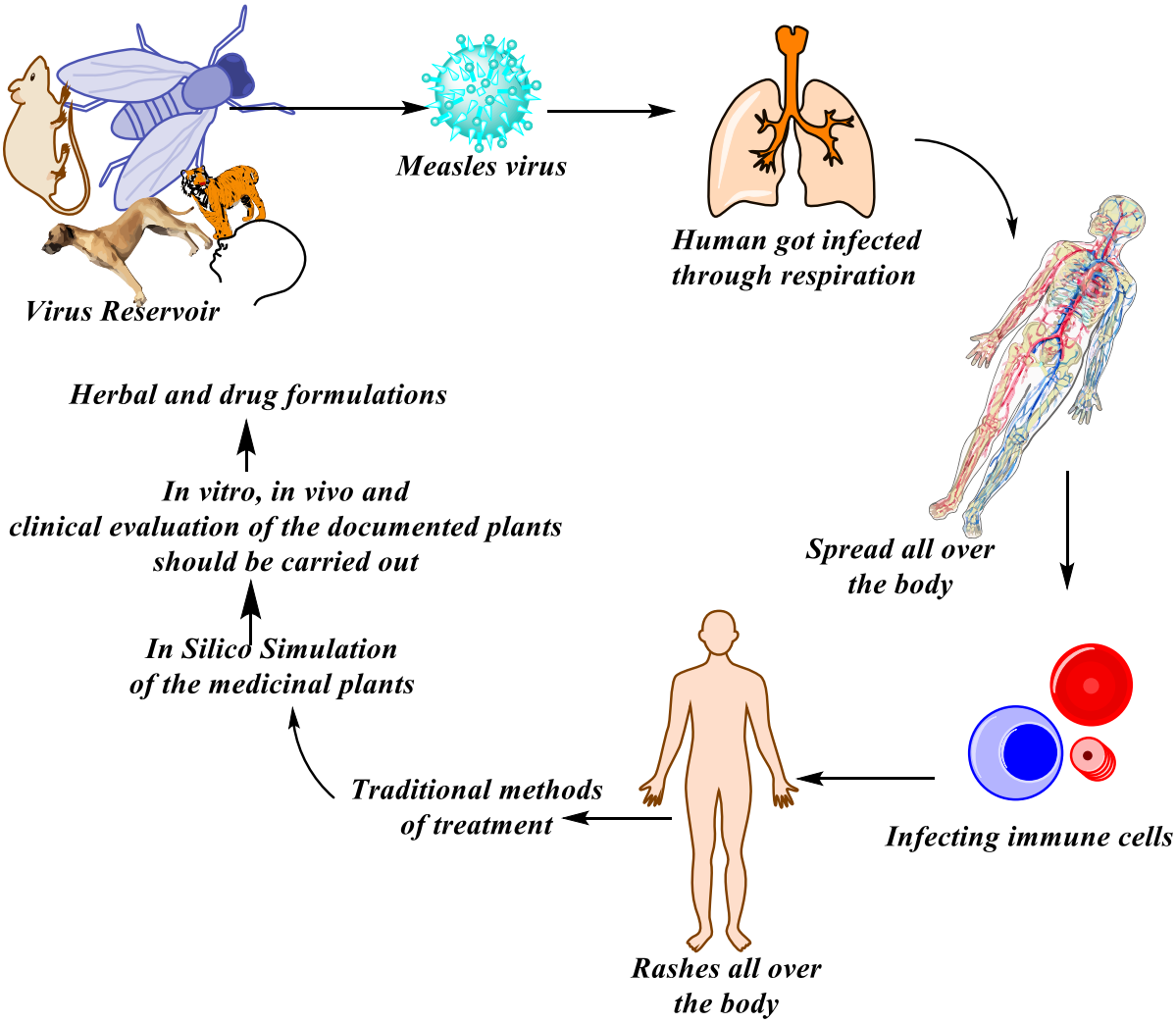

Figure 3. Schematic representation of how a MV infected human can get cured by traditional herbalists and further validated using in silico. The figure suggests that in vitro, in-vivo, and clinical evaluation should be carried out on the documented plants to enable the formulation of herbal drugs and pharmaceutical drugs.

Table 1. Traditional approaches and medicinal plants documented for the treatment and management of measles virus

Family	Botanical name	Hausa name	Part of the plant, method of preparation and administration	Other major diseases treated	Voucher number
Amaranthaceae	*Amaranthus spinosus* L.	Zarangade	Squeeze the leaves mixed with coconut oil and apply to the body and a drop of the extract once daily.	Malaria, inflammation, typhoid, Diabetes	ABUO7210
Amaranthaceae	*Celosia trigyna* L.		Decoction of whole plant and applied to the body.	Menstrual pain, skin disease, diarrhea	ABU05127
Anacardiaceae	*Sclerocarya birrea* (A. Rich.) Hochst.	Danya	Decoction of the bark. Birthing and drinking extract daily.	Cough, wound	ABU0531
Apocynaceae	*Anisopus mannii* N.E. Br.	Kashe Zaki	Decoction of the whole plant. Birthing and drinking of the extract.	Diabetes, hypertension	ABU06123
Asparagaceae	*Chlorophytum laxum* R. Br.	Farin albasa	Decoction of the leaves mixed one tablespoon with one teaspoon of honey and took once daily. Decoction of the root and birthing with the extract twice daily.	Jaundice, skin diseases	ABU0671
Burseraceae	*Boswellia dalzielii* Hutch.	Ararrabi	Decoction of the leaves, bark, and root. Birthing with the extract. Drinking the extract as water.	Stomachache, constipation, malaria, jaundice, all kind of children diseases	ABU0871
Caricaceae	*Carica papaya* L.	Gwanda	Boiled fresh leaves, birthing twice with the extract. Drink the extract as your water.	Malaria, typhoid, fibroid	ABU762
Clusiaceae	*Garcinia kola* Heckel	Namijin Goru	Squeeze the seed and give a drop of the extract on the infected area. While the powders of the seed is mixed with oil or vaseline and apply on the body.	Fibroid, sex enhancer, cold	ABU0728
Combretaceae	*Combretum micranthum* G. Don	Geza	Decoction of the leaves and fruit. Birthing and drinking the extract.	Jaundice, skin diseases, wound	ABU1203
Compositae	*Artemisia annua*	Tazargade	Decoction of the leaves. Birthing and drinking of the extract.	Hypertension, malaria, diabetes	ABU0817
Compositae	*Vernonia amygdalina* Delile	Shuwaka	Wash the leaves to reduce it concentration. Decoction take little as water and apply in the whole body.	Body immune, malaria, jaundice	ABU06601
Cucurbitaceae	*Momordica charantia* L.	Garahuni	Apply the pounded on the rash after making a decoction of fresh fruits and giving a tablespoon of the extract three times a day.	Malaria, body immune, hypertension, typhoid	ABU08062
Fabaceae	*Burkea africana* Hook.	Makarho	Make decoction of the leaves, drink and apply the powder to the body.	Malaria, typhoid, fibroid	ABU9003

Fabaceae	*Prosopis africana* (Guill. & Perr.) Taub.	Kirya	Make decoction of the leaves or bark, drink the extract, and apply the powder to the body.	Cancer, inflammation, skin disease	ABU8112
Lamiaceae	*Ocimum americanum* L.	Dododoya	Inhale the boiled extract of the leaves and apply the pounded fresh leaves on the affected area.	Body immune, malaria	ABU01644
Malvaceae	*Sida acuta* Burm. f.	Tsanya	Pounded fresh whole plant is combined with the oil of *N. sativa* and applied to the entire body. Daily, $^1/_3$ of a teaspoon of the decoction leaves is given until the symptoms disappear.	Malaria, Arthritis, Skin diseases	ABU0117
Meliaceae	*Azadirachta indica* A.Juss.	Bedi	Boiled leaves. Drop the extract in the infected area and birth three times daily with the extract.	Malaria, jaundice	ABU0866
Moringaceae	*Moringa oleifera* Lam.	Zugale	Powdered leaves mixed with Vaseline or olive oil and fresh leaf infusion and take the supernatant whenever needed	Malaria, body immune, hypertension, typhoid	ABU0381
Poaceae	*Urelytrum giganteum* Pilg.	Jema	Apply the powdered leaves to the body and take two tablespoons three times a day of the concoction mixed with honey.	Inflammation, skin diseases	ABU114
Ranunculaceae	*Nigella sativa* L.	Habbatu suada	Take the oil, decoction of the seed, leaves, drink and birthing daily.	Arthritis, inflammation, hypertension, and children related diseases	ABU01823
Rhamnaceae	*Ziziphus abyssinica* Hochst. ex A. Rich.	Magarya	Make decoction of the leaves, drink and apply the powder to the body.	Inflammation, skin diseases, malaria	ABU0745
Rubiaceae	*Mitracarpus hirtus* (L.) DC	Gogamasu	Squeeze the whole plant and apply the extract all over the affected area.	Any skin related diseases	ABU090156
Santalaceae	*Thesium viride* A.W. Hill	Huntu	Apply the powdered mixed with Vaseline to the rashes. Decoction of powdered and administered extract tablespoon three times a day.	Arthritis, inflammation, hypertension, and children related diseases	ABU0731
Solanaceae	*Solanum lycopersicum* L.	Tomatur	Slice and clean the tongue thrice a day if there's rash in the mouth as a result of measles virus.	Body immune, appetizer	ABU0612
	Cow dung	Kahin shanu	Fresh cow dung roaming to feed on grass, apply the cow dung to the whole body and consume the infuse extract of cow dung as water.		
	Fermented *Sorghum*	Banmi	A drop of the extract and apply the fermented *Sorghum* in the whole body.		
	Palmkernel	Mankwakwa	Oil applied in the whole body and drop once in a day.		

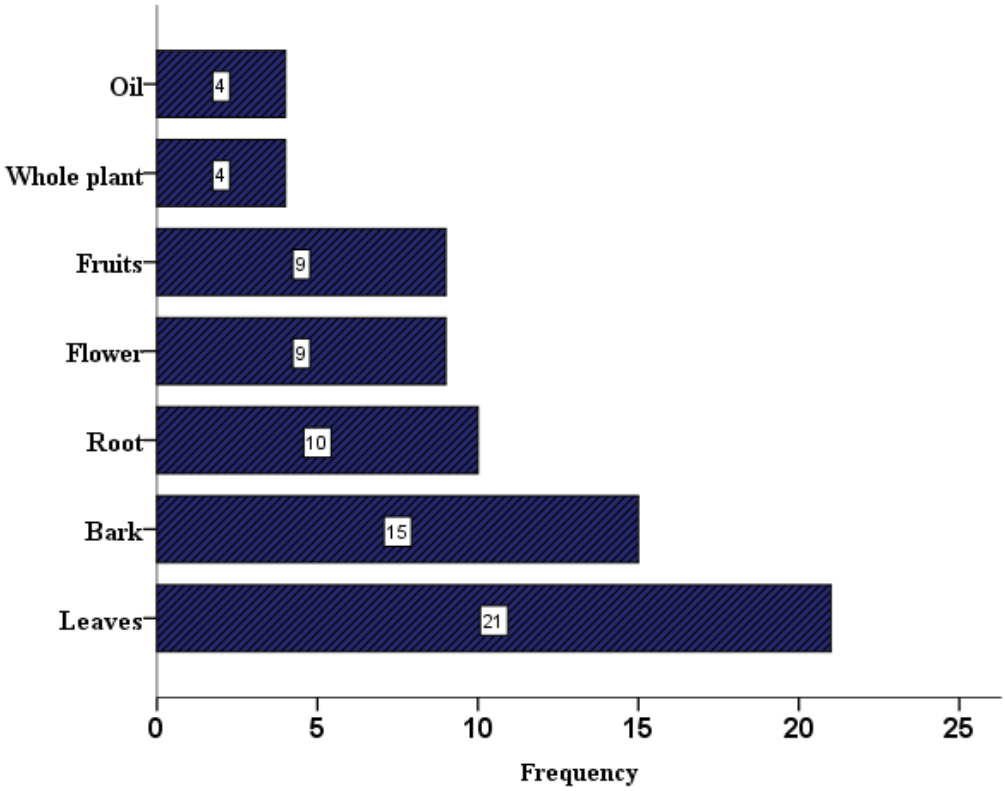

Figure 4. Parts of the plants used for the treatment and management of measles in Northern Nigeria

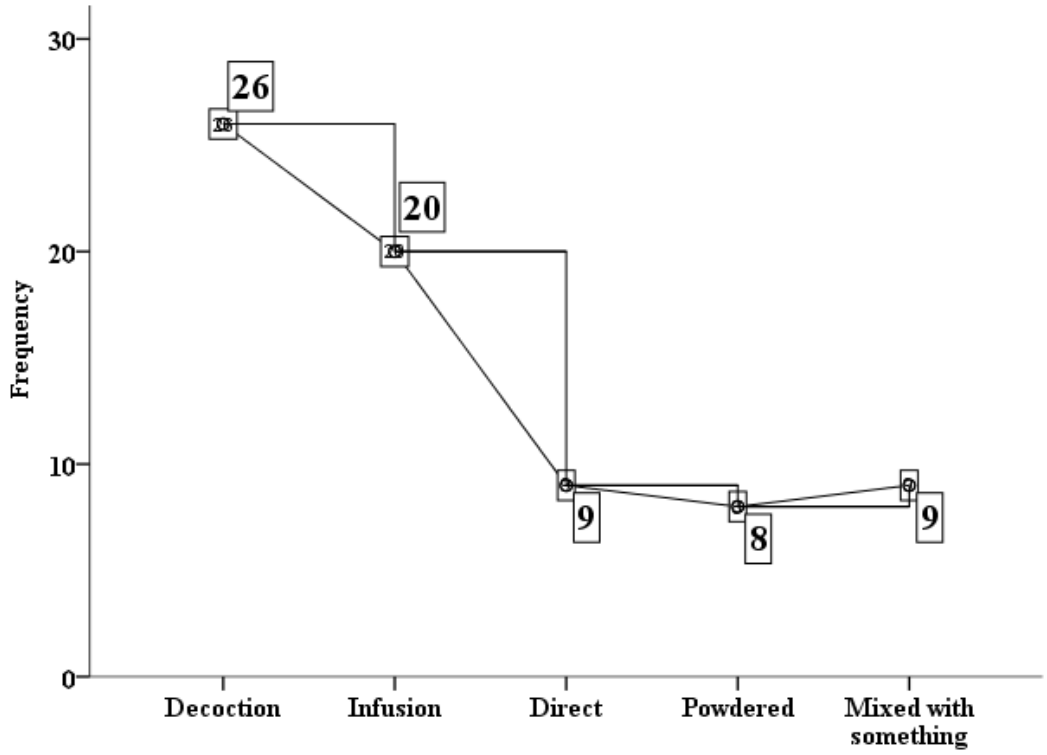

Figure 5. Methods of preparation of medicinal plants used for the treatment and management of measles in Northern Nigeria

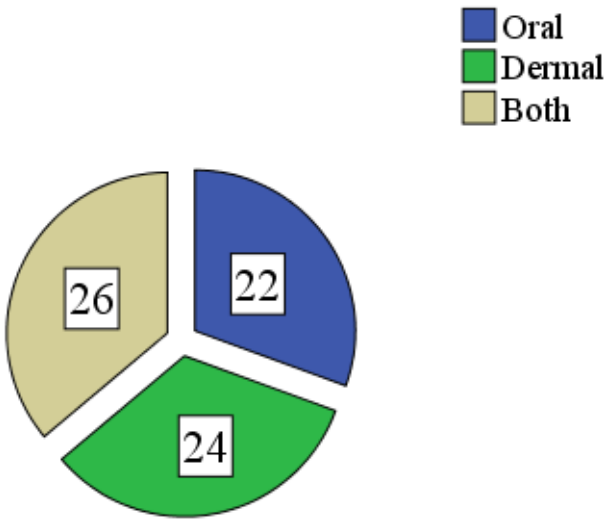

Figure 6. Methods of Administration of medicinal plants used for the treatment and management of measles in Northern Nigeria

Quantitative Evaluation

Quantitively, UV, RFC, and FL were calculated to determine the popularity and effectiveness of the documented plant species used for the treatment of measles. The reported plants (Table 2). The traditional approach was found to be more effective in the management and treatment of measles (Table 2).

Table 2. Quantitative Parameters

Botanical name	Fidelity Level	RFC	Used Value
Anisopus mannii	93.3	0.77	0.08
Amaranthus spinosus	79.1	0.83	0.08
Artemisia annua	51.2	0.51	0.04
Azadirachta indica	79.1	0.63	0.06
Burkea africana	70.1	0.63	0.11
Boswellia dalzielii	64.1	0.73	0.11
Combretum micranthum	75	0.83	0.13
Carica papaya	79.1	0.71	0.08
Chlorophytum laxum	79.1	0.63	0.11
Celosia trigyna	64.1	0.77	0.13
Garcinia kola	70.1	0.73	0.11
Momordica charantia	75	0.77	0.13
Moringa oleifera	75	0.77	0.11
Mitracarpus hirtus	70.1	0.71	0.06
Nigella sativa	75	0.83	0.08
Ocimum americanum	64.1	0.77	0.08
Prosopis africana	70.1	0.77	0.06
Sclerocarya birrea	70.1	0.71	0.13
Solanum lycopersicum	75	0.71	0.07
Thesium viride	64.1	0.83	0.06
Urelytrum giganteum	75	0.63	0.07
Vernonia amygdalina	75	0.63	0.07
Ziziphus abyssinica	64.1	0.77	0.08
Sida acuta Burfi.	64.1	0.63	0.13
Cow dung	100	1	-
Palmkernel	93.3	0.83	-
Fermented *Sorghum*	100	1	-

***In silico* prediction**

The nature of interaction between the investigated compounds and the measles virus nucleoprotein core in complex with an n-terminal region of phosphoprotein (pdb entry code: **5E4V**) was studied using molecular docking-based virtual screening to identify compounds with higher affinity toward the target enzyme. Table 3 shows the binding affinities of the investigated compounds. The binding affinities of the investigated compounds range from -1.3 Kcal/mol to -9.3 Kcal/mol, respectively.

Table 3. The binding affinities of the investigated compounds

Ligand	Binding Affinity (kcal/mol)
Chlorophytum laxum	
25R-spirosta35dien12ol(1)	-8.7
Anisopus mannii	
Hexadecanoic_acid_ethyl_ester	-5.6
Oxirane	-5.2
Amaranthus spinosus	
24-ethyl-lanostane	-8.2
Atropine	-6.9
Sclerocarya birrea	
Terpinen-4-ol	-5.7
Pyrrolidine	-3.2
Boswellia dalzielii	
Alpha-Pinene	-5
Celosia trigyna	
Quercetin3Orhamnosy	-8.5
Amyrin_acetate	-8.9
Combretum micranthum	
()-catechin	-7.7
Gallic_acid	-6
Garcinia kola	
Biflavonoids	-8.3
Garcinoic_Acid	-7.9
Vernonia amygdalina	
Caryophyllene	-7
(E)farnesene	-7.1
Carica papaya	
Vitamin_C	-6.5
Momordica charantia	
Momorcharin	-7.3
Charine	-6.5
Prosopis africana	
Flavonoic	-8.3
Phenol	-4.6
Burkea africana	
(13a)_Caffeic_acid	-6.4
(13b)_Rutin	-8.5
Ocimum americanum	

Geranial	-5.4
Linalool	-4.9
Carvacrol	-6.4
Moringa oleifera	
Alkaloid_trigonelline	-4.8
Sesquiterpenoid_abscisic	-6.3
Caffeic_acid	-6.4
Caffeic_acid	-8.5
Azadirachta indica	
Kaempferol-3-Orutinoside	-8.2
Epicatechin	-7.7
Sida acuta	
Cryptolepine	-7.1
Quinoline	-1.3
Mitracarpus hirtus	
Quinoline	-9.3
Nigella sativa	
Thymoquinone	-5.9
Zizphus abyssinica	
Amyrin	-9.3
Polpunonic_acid	-8.7
Thesium viride	
Anthraquinones	-7
Saponin	-9

Quinoline was the compound with the highest binding affinity of -9.3Kcal/mol among the investigated compounds interacting with the binding pose of 5e4v-receptor via 12 hydrophobic interactions with the following amino acid residues VAL157 (3), ARG175 (5), LEU158, LEU197 and LYS179 (2), respectively (Table 4). Beside Quinoline, Amyrin had also -9.3 Kcal/mol binding affinity which interacted with virtually almost the same amino acid residues as Quinoline. Figure 7 presents the 2D structures of Quinoline and Figure 8 Amyrin in complex with 5e4v-receptor.

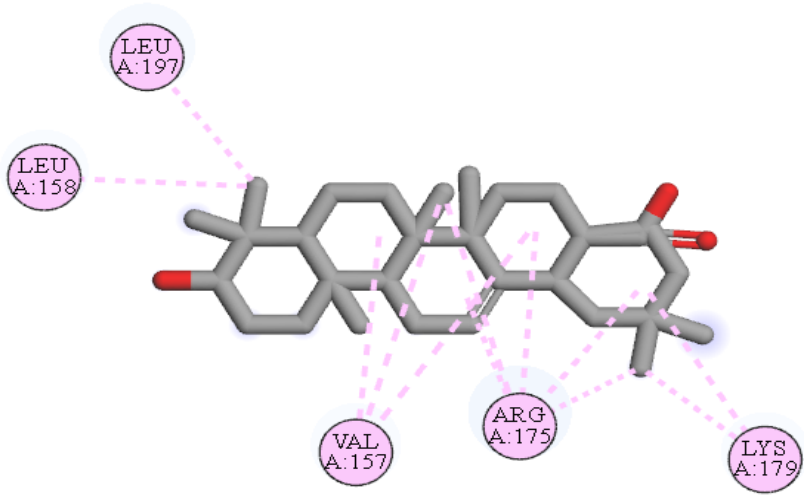

Figure 7. Quinoline in complex with 5e4v-receptor

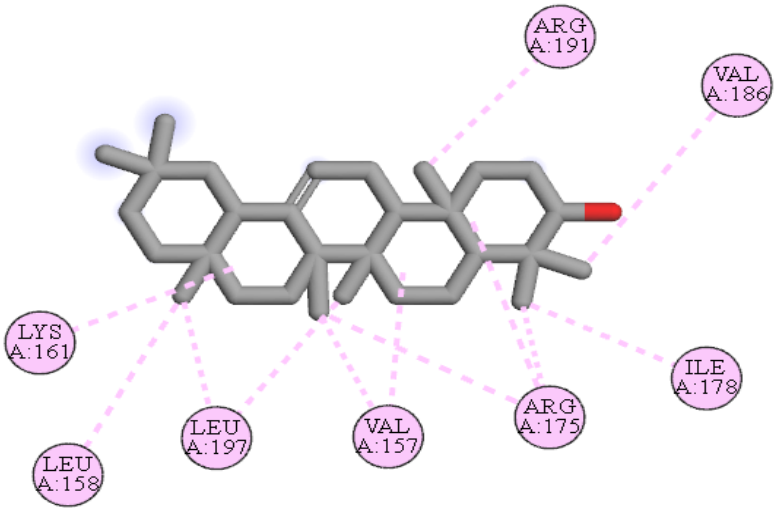

Figure 8. Amyrin in complex with 5e4v-receptor

The second compound with high binding affinity among the investigated compounds Saponin (-9.0 Kcal/mol). The nature of interaction between Saponin and the binding pose of 5e4v-receptor was via hydrophobic with LEU197, ARG175 (5), LYS179, ALA153, VAL157, ILE178, LYS179, VAL186 amino acid residues respectively. Figure 9 presents the 2D structure of Saponins in complex with 5e4v-receptor.

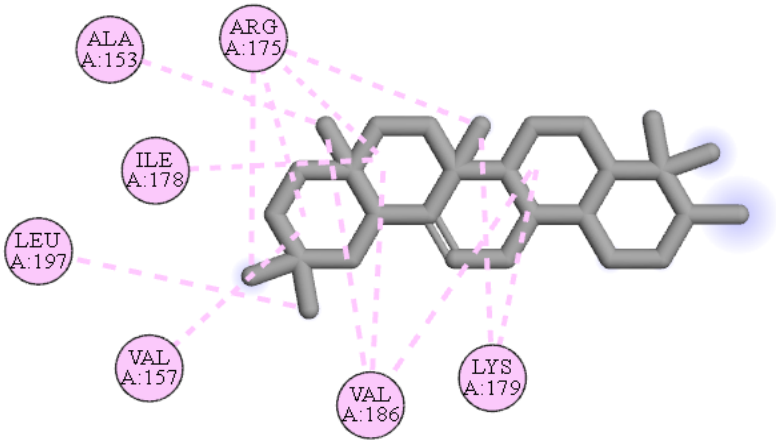

Figure 9. Saponin in complex with 5e4v-receptor

Amyrin-acetate with a binding affinity of -8.9 kcal/mol formed hydrophobic interaction with LYS161, LEU197, VAL157 (3), ARG175 (4), LYS179 (2), VAL186 (2) and ILE178 amino acid residues in the binding pose of 5e4v-receptor as shown in Table 4, respectively. Figure 10 presents the 2D structure of Amyrin_acetate in complex with 5e4v-receptor.

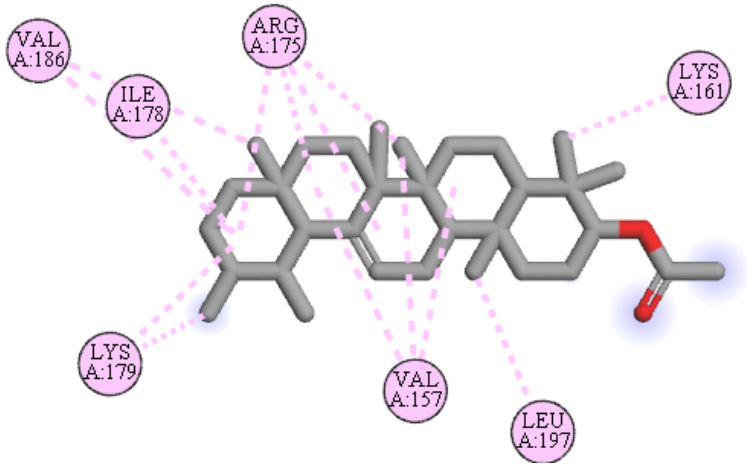

Figure 10. Amyrin_acetate in complex with 5e4v-receptor

The nature of interactions of (1)25R-spirosta35dien12ol(1) with the binding pose of 5e4v-receptor via hydrogen bond with ASN42 amino acid residues and hydrophobic interaction with TRP127, ARG35, ARG38 & PHE112 amino acids as shown in Table 4, respectively. The 2D structure of 25R-spirosta35dien12ol(1) in complex with 5e4v-receptor is shown in Figure 11.

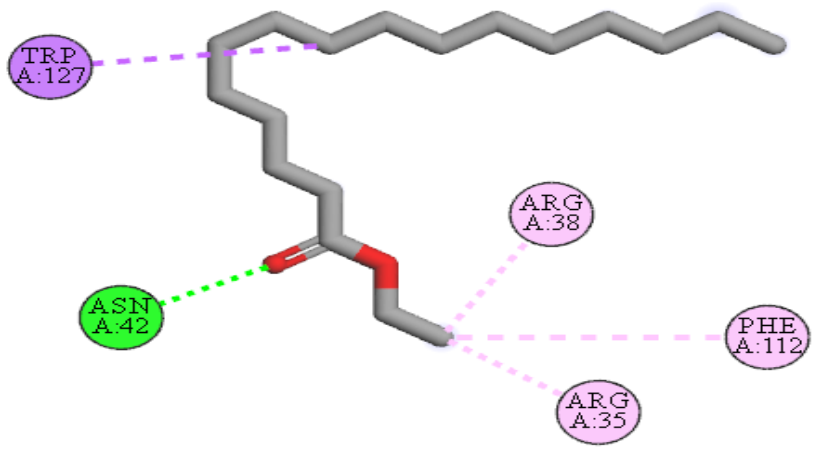

Figure 11. 25R-spirosta35dien12ol(1) in complex with 5e4v-receptor

Polpunonic-acid with a binding affinity of -8.7 kcal/mol interacted with the binding pose of 5e4v-receptor via two (2) hydrogen bonds with ARG191 amino acids and through hydrophobic interaction with LEU197, VAL186 (2), VAL157 (3), ARG175 (5), ILE178 & ALA153 (2) amino acid residues as presented in Table 4, respectively. The 2D structure of Polpunonic_acid in complex with 5e4v-receptor is shown in Figure 12.

Table 4. Binding affinities and nature of interactions of the most potent compounds.

Code	Binding affinity	Hydrogen bond	Hydrophobic interactions
Quinoline	-9.3		VAL157 (3), ARG175 (5), LEU158, LEU197, & LYS179 (2)
Amyrin	-9.3		LEU158, LEU197 (2), ARG191, VAL157 (2), VAL186, ILE178, LYS161 & ARG175 (3)
Saponin	-9.		LEU197, ARG175 (5), LYS179, ALA153, VAL157, ILE178, LYS179, VAL186 (3)
Amyrin-acetate	-8.9		LYS161, LEU197, VAL157 (3), ARG175 (4), LYS179 (2), VAL186 (2) & ILE178
25R-spirosta35dien12ol(1)	-8.7	ASN42	TRP127, ARG35, ARG38 & PHE112
Polpunonic-acid	-8.7	ARG191 & ARG191	LEU197, VAL186 (2), VAL157 (3), ARG175 (5), ILE178 & ALA153 (2)

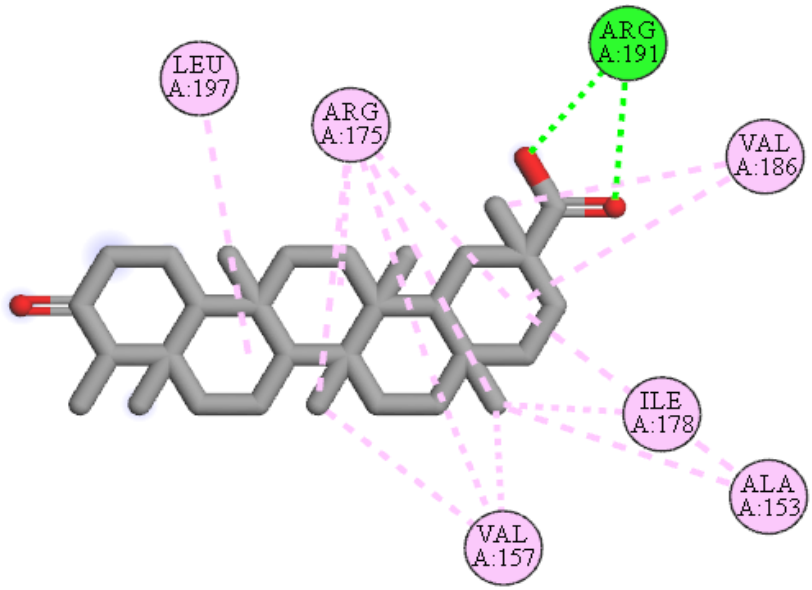

Figure 12. Polpunonic_acid in complex with 5e4v-receptor

Discussion

Measles has no particular therapy. In contrast to bacterial infections, viral infections are not susceptible to antibiotic treatment. Typically, the virus and associated symptoms resolve within two to three weeks. Apart from immunization, the following medications are used to treat measles: acetaminophen (Tylenol), ibuprofen (Advil) to lower fever, and vitamin A supplements. Acetaminophen is a member of the family of medicines known as analgesics. Ibuprofen is a member of the family of medications known as nonsteroidal anti-inflammatory medicines (Cramer *et al.*, 2021). Ibuprofen decreases pain and inflammation; also, the plants surveyed were found to have antiinflammation, indicating that they could be used to manage measles. Most of the plants documented possess carotenoids and antioxidants potentials that could play a vital role in the management of measles. This could validate the use of the selected plant to treat measles in Northern Nigeria. The present study adopted a method of purposive sampling. The study follows a similar train of research carried out on traditional medicinal knowledge in the region (Dogara *et al.*, 2021; Mahmoud *et al.*, 2020). According to the interviewees, men's dominance in the study was attributable to the culture and religion of the studied area, where women are usually restricted to their homes and do not have access to the forest (Wali *et al.*, 2021). The majority of the respondents only attended primary basic education. Western education was seen as a secondary option not needed for traditional occupations. Our findings are consistent with earlier studies in the region (Zakariya *et al.*, 2021). The dominance of 30-49-year-olds is due to the fact that they are in their most active professional stage and hence devoted more time to the interview and field collection. The dominancy of this relatively young age class age demonstrates the transmission of traditional medicinal knowledge in the region. Respondents believed that plant material collected from the wild in the forest was more effective than the same species occurring in gardens. Leaves were utilized more frequently than other parts of medicinal plants, similar to other areas of the region and other parts of the world (Dogara *et al.*, 2021; Mahmoud & Abba, 2021). The prevalence of leaves may be due to the fact that they are easier to collect and that secondary metabolites are primarily produced there. From a conservation standpoint, the usage of leaves is safer and more sustainable (Abdulrahman *et al.*, 2018). The decoction was the most frequently used method of preparation of medicinal plant parts for the treatment and management of measles in the region. The respondents believed that a decoction collects the plant content in a short period of time. Both oral and dermal applications were important, in line with the manifestation of the disease. Drug-ability/drug likeness provides the criteria for a particular chemical compound or drug in terms of its potency or efficiency. The absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties, also known as pharmacokinetics properties, describe the fate of a drug/small molecule in the body of a living organism (Li G, Shao, & Umeshappa, 2019; Lipinski, 2004; Olasupo *et al.*, 2020). From the results of the docking-based virtual screening, Quinoline and Amyrin were identified as having the highest binding affinity of -9.3 Kcal/mol among the other investigated compounds, followed by Saponins with a binding affinity of -9.0 Kcal/mol, Amyrin_acetate with a binding affinity of -8.9 Kcal/mol, (1)25R-spirosta35dien12ol(1) and Polpunonic_acid each with a binding affinity of -8.7 Kcal/mol, respectively. As a result, this study backs the usage of herbal folk medicine as anti-measle therapy because all plants used to treat the disease were found to have either analgesic, antimicrobial, antioxidant, and anti-inflammatory compounds. There

is a need of further investigation on the reported plants because they hold some mystery. Toxicity, mechanism of action, and dosage need to be determined.

Conclusion

The current investigation documented therapeutic plants with high RFC and FL values, indicating that people in Northern Nigeria have long used these species to treat measles. The respondents' claims were validated by the results obtained *in silico* by showing the plants to exhibit activity against measles virus, with especially plants containing quinoline compounds having high activity. The study also reported fresh cow dung being the most popular measles treatment method in the whole region. It would be interesting to evaluate this application, as well as extracts of the plant species employed, further *in vitro*, *in vivo,* and clinal evaluation so that it can be transformed into effective, safe, and economical anti-measles herbal and pharmaceutical drugs in the future.

Declarations

List of abbreviations: RFC = Relative Frequency of Citation, FL = Fidelity Level, UV = Used Value. MDA = Mahmoud Dogara Abdulrahman, SWB = Sarwan W. Bradosty, SWH = Saber W. Hamad, MTI = Muhammad Tukur Ibrahim, AAL = Abubakar Abdullahi Lema, NS = Namadi Sunusi, MU = Muhammad Usman, IA = Ibrahim Ashiru, NBA = Nuraddeen Bello Ahmad, NW = Nuradeen Wada, RWB = Rainer W. Bussmann

Ethics approval and consent to participate: Ethical approval was given by the ethical committee of Al-Qalam University, Katsina, Katsina state, Nigeria (AQUDBEC/2021/012). The responders' verbal consent was sorted. The informants were fully informed of the study's objectives and provided oral prior informed consent,

Consent for publication: Not applicable.

Competing interests: There are no competing interests.

Authors contributions: MDA = Drafted proposal , SWB = Checking and , SWH = Checking, MTI = Molecular Docking, AAL = Literature Search, NS = Herbarium Specimen Preparation, MU = Field Collection and Interview, IA = Field Collection and Interview , NBA = Field Collection and Interview, NW = Field Collection and Interview, RWB = Revision and amending of the draft manuscript.

Data Availability: All data are available in the manuscript

Conflict of interest: Authors declare no conflict of interest

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