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(Research Article)

Inorganic and organic chemical constituents of trona, alum and palm ash: Potential alternatives to conventional antifungal drugs?

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Abstract

There is high demand for the development of novel, effective, clinically safe and affordable antifungal agents to manage the ever emerging and re-emerging fungal infections. Natural compounds may be a source of novel chemical structures for development of antimicrobials. The aim of this study was to determine the inorganic and organic chemical constituents of trona, alum and palm ash; as potential alternatives to conventional antifungal drugs. The fungal isolates were obtained from high vaginal swab samples of patients suffering from vulvo-vaginal candidiasis. The isolates were identified based on their macroscopic, physiological, biochemical and molecular characteristics. The minimal inhibitory concentration (MIC) and minimal fungicidal concentrations (MFC) of the test agents were determined using the broth dilution method. Gas chromatography-mass spectroscopy (GC-MS) was used to determine the organic constituents; while x-ray fluorescence spectroscopy, for inorganic constituents. The isolates include *Candida albicans, C. tropicalis, C. glabrata* and *C. parapsilosis.* The MIC and MFC of alum against the isolates ranged from 12.50 mg/ml to 50 mg/ml, trona (6.25 mg/ml to 100 mg/ml) and palm ash (100 mg/ml to 200 mg/ml). Alum comprises oxides of sulphur (44.5 %), aluminium (14.49 %) while lead, arsenic and nickel all accounted for <0.0010 %. The naturally occurring fatty acids include vaccenic acid (40.39 %), decanoic acid (13.21 %) and linoelaidic acid (9.84 %). Trona comprises of sulphur (2.14 %), chlorine (5.8 %), potassium (1.7 %), lead (0 %), arsenic and nickel (<0.003 %); while the organic constituents include linoelaidic acid (32.99 %), nonanoic acid (14.81 %) and decanoic acid (6.8 %). The inorganic components of palm ash include potassium (28.8 %), sulphur (3.4 %), calcium (2.8 %) and chlorine (15 %) while the heavy metals all accounted for <0.0007 %. The organic constituents were urea (8.65 %) and fatty acids (<6 %). The antimicrobial properties of the natural compounds were probably due to their various organic and inorganic constituents; thus, could serve as potential raw materials in antifungal drugs production.

Keywords: Antifungal; Novel; Trona; Alum; Palm ash

1. Introduction

Fungal pathogens are responsible for at least 13 million infections and 1.5 million deaths globally per year, primarily in immunocompromised individuals. In these patients, infections can quickly become severe, resulting in high morbidity and mortality (Bongomin *et al.*, 2017). Mycoses are classified as superficial, cutaneous, subcutaneous, or systemic (deep) infections depending on the type and degree of tissue involvement and the host response to the pathogen. Superficial mycoses are limited to the stratum corneum and essentially elicit no inflammation. Cutaneous infections involve the integument and its appendages, including hair and nails (Odds *et al*., 1992; Walsh *et al*., 1995 and McGinnis, 1980).

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Infectious diseases caused by fungal pathogens, such as aspergillosis, candidiasis, or cryptococcus, are recurring problems. Current antifungal interventions often exhibited very limited efficacy in treating fungal infections, partly because the spectrum of activity of conventional systemic antifungal drugs is narrow while the development of new antifungal drugs has become stagnant. Azole and polyene drugs were introduced before 1980, whereas the echinocandin drug CAS was approved for the clinical uses since 2000 (Roemer and Krysan, 2014).

Host toxicity, cost, emergence of resistance and difficulty in developing new selective antifungals pose challenges in management of fungal infections (da Costa *et al*., 2015). The toxicity triggered by conventional antifungal drugs also hampered the effectiveness of antifungal therapy. For example, the polyene, amphotericin B (AMB) was the first antifungal drug introduced to clinical settings more than fifty years ago. However, AMB also triggered varying toxicity to the hosts, such as infusion-related reactions, nephrotoxicity etc. Therefore, different types of formulations have been developed, for instance, lipid-associated AMB formulations such as the AMB lipid complex (AMB-LC), liposomal AMB (L-AMB) and colloidal dispersion of AMB (AMB-CD) (Hamill, 2013).

As fungi share many conserved cellular functions with potential host eukaryotes (humans, plants), the discovery of effective antifungal drugs or fungicides is challenging while resistance is growing to existing agents, accentuating the need for discovery of novel measures for fungal control (Roemer and Krysan, 2014; *Fisher et al*., 2018). The need for new antifungals has therefore prompted a screen for better alternatives to the conventional antifungal agents. Many natural products (NPs) possess antifungal activity. NPs have been used since historical times to control the spread of fungal diseases, infections, and food contamination. Bioactives derived from NP according to the origin could be classified as (i) unregulated natural substances, (ii) NPs not modified and regulated by the Food and Drug Administration (FDA), (iii) chemically modified natural compounds (also called semi-synthetic), and (iv) a synthetic compound that copies a natural (mimetic) compound (Patridge *et al*., 2016).

Potassium carbonate otherwise called trona, akanwu or kanwa is a yellowish – white or grayish – white alkaline salt, soluble in water and insoluble in alcohol or acetone. It forms a strongly alkaline solution when dissolved in water. Potassium carbonate was first identified by Antonio Campanella in 1742. It has been used and mined for hundreds of years for several different purposes. Other terms for potassium carbonate include: carbonate of potash, dipotassium carbonate, dipotassium salt, pearl ash, "potash", salt of tartar, or salt of wormwood. Today, potassium carbonate is prepared commercially by the electrolysis of potassium chloride. The resulting potassium hydroxide is then carbonated using carbon dioxide to form potassium carbonate which is often used to produce other potassium compounds (Bulatovic, 2015; Civitello, 2017). Today, in addition to the large market for glass, soda ash produced from trona is used in the production of chemicals, paper, detergents, textiles and water treatment products (Dini and Jones, 1998). Several health benefitsof potash have been unraveled. It has been used for the treatment of cough, tooth ache relief, fungicidal, abortifacient and as a preservative (Rabiu and Malami, 2019).

Alum is an inorganic chemical compound that is generally made up of water molecules, aluminum or other metals and sulphates. Alum is basically a hydrated double sulphate salt of aluminum.The general chemical formula for alum is XAl(SO4)2·12H2O whereby X is a monovalentcation such as potassium or ammonium. By itself, "alum" is often refers to potassium alum, with the formula KAl(SO4)2·12 H2O. Other alums are named after the monovalent ion, such as sodium alum and ammonium alum. Alums can occur as minerals. For example, alunite and leucite. It is found in nature in both pure and impure forms and is obtained from the soil ore found in Nepal, Bihar, Punjab, and the Kathiawar area. Alum is a colourless, clear, odourless, crystalline mass or granular powder with a sweetish astringent flavour. It is also found in Egypt, Italy, England, Germany and India (Rice, 1957; Li *et al*., 2017; Austin, 1984; Vignesh *et al*., 2019). The resourcefulness of Alum individually or in synergism as food preservative, medicine, water purifier, biotransformational and antimicrobial agents and sundry applications had been well documented (Amadi, 2020).

Palm bunch ash (PBA), traditionally known as ngu in south eastern Nigeria, is used in place of trona (Akanwu) as food additive and tenderizer. It is also believed to be a non-purgative substance in preparing crude palm oil and African salad popularly known as Abacha. PBA produced by burning or ashing, which constitutes about 6.5% by weight of the empty fruit bunch (Okoye *et al.,* 2016), contains 30–40% K_2O and could thus be used as source of potassium fertilizer. PBA has high pH and contains varying amounts of other nutrients such as calcium (Ca), phosphorus (P), and magnesium (Mg) (Okoye *et al.,* 2016). Palm ash has been established to possess antimicrobial properties against *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Proteus sp, Staphylococcus aureus*, *Aspergillus fumigates, Candida albicans*, *Candida pseudotropicalis and Penicillium expansuim* (Ntukidem *et al.,* 2020).

The aim of this study was to determine the inorganic and organic chemical constituents of trona, alum and palm ash; as potential alternatives to conventional antifungal drugs.

2. Materials and Methods

2.1. Study area

This study was carried out at the Laboratory Unit of Department of Applied Microbiology and Brewing, Nnamdi Azikiwe University, Awka, Anambra State, South-East geopolitical zone of Nigeria. It is located between latitude $6^{o}20''00''$ North and Longitude $7^{o}00''00''$ East. The average temperature is $25.9^{o}C$ while the average rainfall in a year is 1386mm.

2.2. Samples Collection

The samples trona, alum and palm ash were hygienically selected and purchased at the Eke-Awka market in Awka South Local Government Area of Anambra State, Nigeria. They were transferred into sterile containers and transported to the laboratory for analysis. The method described by Kamka-Evans *et al*. (2013) was adopted.

2.3. Isolation and Identification of the fungal organisms

The yeast isolates were obtained from high vaginal swab samples and identified based on their macroscopic, physiological, biochemical and molecular characteristics (Udemezue and Oyeka, 2021).

2.4. MIC and MFC Determination using the Broth Dilution Method

Various concentrations of the test agents were made in Sabouraud dextrose broth by double fold serial dilution to obtain 200 mg/ml, 100 mg/ml, 50 mg/ml, 25 mg/ml, 12.25 mg/ml, 6.325 mg/ml, 3.125 mg/ml and 1.5625 mg/ml. Each dilution in a test-tube was inoculated with 0.2 ml of the broth culture of test isolates (0.5 McFarland standards). All the tubes were incubated at 25 °C for 24 hours. The lowest concentration showing no visible growth (as compared with a negative control) was recorded as the minimum inhibitory concentration (MIC) for each organism (Cheesbrough, 2018).

The MFC was determined by transferring 0.2 ml from each negative tube in MIC assay, onto the surface of freshly prepared Sabouraud dextrose agar plates using the spread plate method and incubated at 25°C for 48 hrs. The lowest concentration showing no visible growth on SDA was recorded as minimum fungicidal concentration (MFC) for each organism (Cheesbrough, 2018).

2.5. Chemical Constituents Analysis

2.5.1. Gas Chromatography-Mass Spectroscopy (GC-MS) for organic constituents' analysis

The GC–MS analysis of the solutions was done using Agilent Technologies GC systems with GC-7890A/MS-5975C model (Agilent Technologies, Santa Clara, CA, USA) equipped with HP-5MS column (30 m in length × 250 μm in diameter × 0.25 μm in thickness of film). Spectroscopic detection by GC–MS involved an electron ionization system which utilized high energy electrons (70 eV). Pure helium gas (99.995 %) was used as the carrier gas with flow rate of 1 mL/min. The initial temperature was set at 50 –150°C with increasing rate of 3°C/min and holding time of about 10 min. Finally, the temperature was increased to 300 °C at 10 °C/min. One microliter of the prepared 1% of the sample diluted with respective solvents was injected in ansplitless mode. Relative quantity of the chemical compounds present in each of the samples was expressed as percentage based on peak area produced in the chromatogram. Bioactive compounds in the various solutions were identified based on GC retention time on HP-5MS column and matching of the spectra with computer software data of standards (Replib and Mainlab data of GC–MS systems) as described by Buss and Butler (2010).

2.5.2. X-Ray fluorescence spectroscopy for inorganic constituents' analysis

The samples size was first reduced to meet a ~10-μm particle size fraction. Once in powdered form, the sample was packed into a sample tray and analyzed by XRF. The XRF analysis provides a quantitative data for a suite of minerals. Identification of minerals is based on the location and intensity of peaks on the 2θ scale. Samples prepared were scanned with a Scintag® XFS2000 X-ray fluorescence using CuKα radiation at 40 kV and 30 mA. The majority of the scans were performed using a continuous scan mode from 2 to 34° 2θ with a 0.05 step size at 2 degrees per minute. The collected data were then analyzed using Jade 9+® software. To conclude the process, the results were assembled into easy-to-read spreadsheets, and the XRF trace for each sample was put into the form of a jpg image as described by Maddix *et al*. (2002).

3. Results

Table 1 MIC determination of all the test agents against *Candida albicans* using broth dilution method

Concentration (mg/ml)	Alum	Trona	Palm ash	Ketoconazole (Control)
1.56	+	+	+	+
3.13	+	+	+	+
6.25	+	+	+	+
12.50	+	+	+	+
25	+	+	+	+
50	-	+	+	-
100	-	-	-	-
200	-	-	-	-

+Presence of growth; -No visible growth

Table 2 MIC determination of all the test agents against *Candida tropicalis* using broth dilution method

Concentration (mg/ml)	Alum	Trona	Palm ash	Ketoconazole (Control)
1.56	+	+	+	+
3.13	+	+	+	+
6.25	+	+	+	+
12.50	+	+	+	+
25	-	+	+	-
50	-	-	+	-
100	-	-	-	-
200	-	-	-	-

+Presence of growth; - No visible growth

Table 3 MIC determination of all the test agents against *Candida glabrata* using broth dilution method

Concentration (mg/ml)	Alum	Trona	Palm ash	Ketoconazole(Control)
1.56	+	+	+	+
3.13	+	+	+	+
6.25	+	-	+	+
12.50	-	-	+	+
25	-	-	+	+
50	-	-	+	-
100	-	-	-	-
200	-	-	-	-

+Presence of growth; - No visible growth

Table 4 MIC determination of all the test agents against *Candida parapsilosis* using broth dilution method

Concentration (mg/ml)	Alum	Trona	Palm Ash	Ketoconazole(Control)
1.56	+	+	+	+
3.13	+	+	+	+
6.25	+	-	+	+
12.50	-	-	+	-
25	-	-	+	-
50	-	-	+	-
100	-	-	-	-
200	-	-	-	-

+Presence of growth; - No visible growth

Table 5 MFC determination of all the test agents against *Candida albicans* using broth dilution method

Concentration (mg/ml)	Alum	Trona	Palm ash	Ketoconazole(Control)
1.56	+	+	+	+
3.13	+	+	+	+
6.25	+	+	+	+
12.50	+	+	+	+
25	+	+	+	+
50	-	+	+	-
100	-	-	-	-
200	-	-	-	-

+Presence of growth; - No visible growth

Table 6 MFC determination of all the test agents against *Candida tropicalis* using broth dilution method

Concentration (mg/ml)	Alum	Trona	Palm ash	Ketoconazole(Control)
1.56	+	+	+	+
3.13	+	+	+	+
6.25	+	+	+	+
12.50	+	+	+	+
25	+	+	+	-
50	-	+	+	-
100	-	-	+	-
200	-	-	-	-

+Presence of growth; - No visible growth

Table 7 MFC determination of all the test agents against *Candida glabrata* using broth dilution method

Concentration (mg/ml)	Alum	Trona	Palm ash	Ketoconazole (Control)
1.56	+	+	+	+
3.13	+	+	+	+
6.25	+	+	+	+
12.50	-	-	+	+
25	-	-	+	+
50	-	-	+	-
100	-	-	-	-
200	-	-	-	-

+Presence of growth; - No visible growth

Table 8 MFC determination of all the test agents against *Candida parapsilosis* using broth dilution method

Concentration (mg/ml)	Alum	Trona	Palm ash	Ketoconazole(Control)
1.56	+	+	+	+
3.13	+	+	+	+
6.25	+	+	+	+
12.50	+	+	+	+
25	-	-	+	-
50	-	-	+	-
100	-	-	+	-
200	-	-	-	-

+Presence of growth; - No visible growth

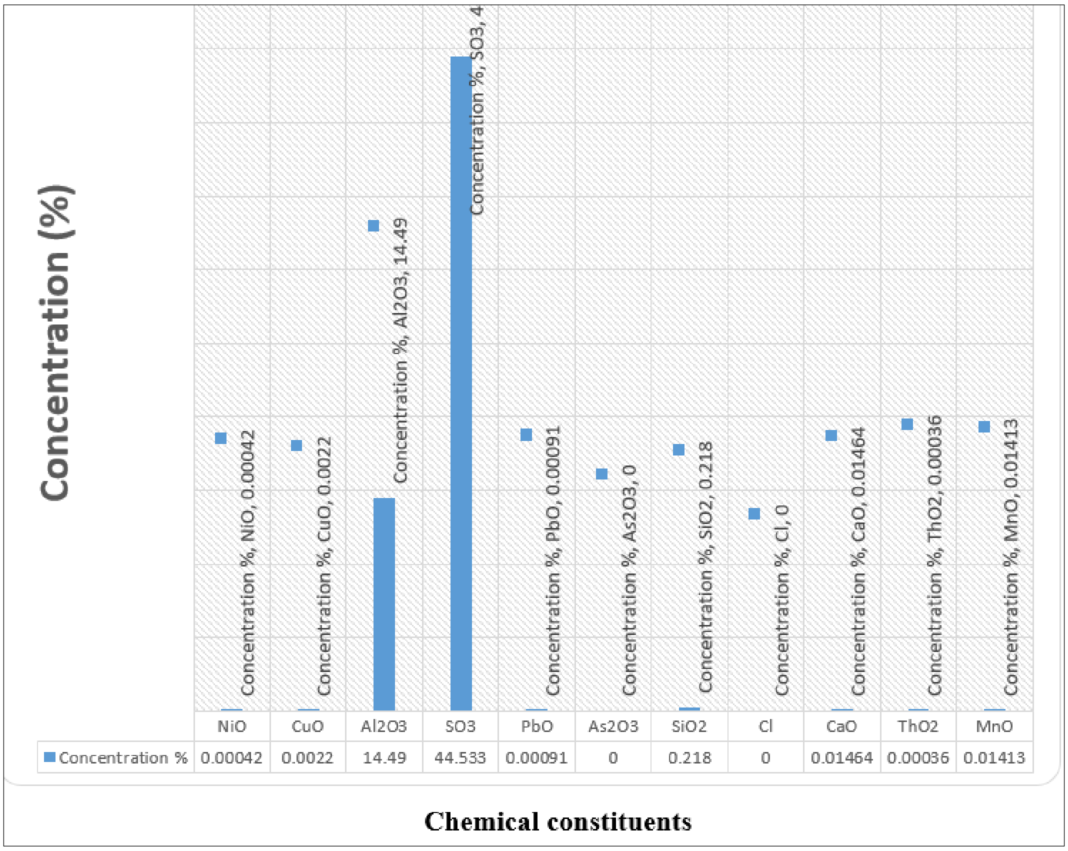

Figure 1 Inorganic chemical constituents of Alum

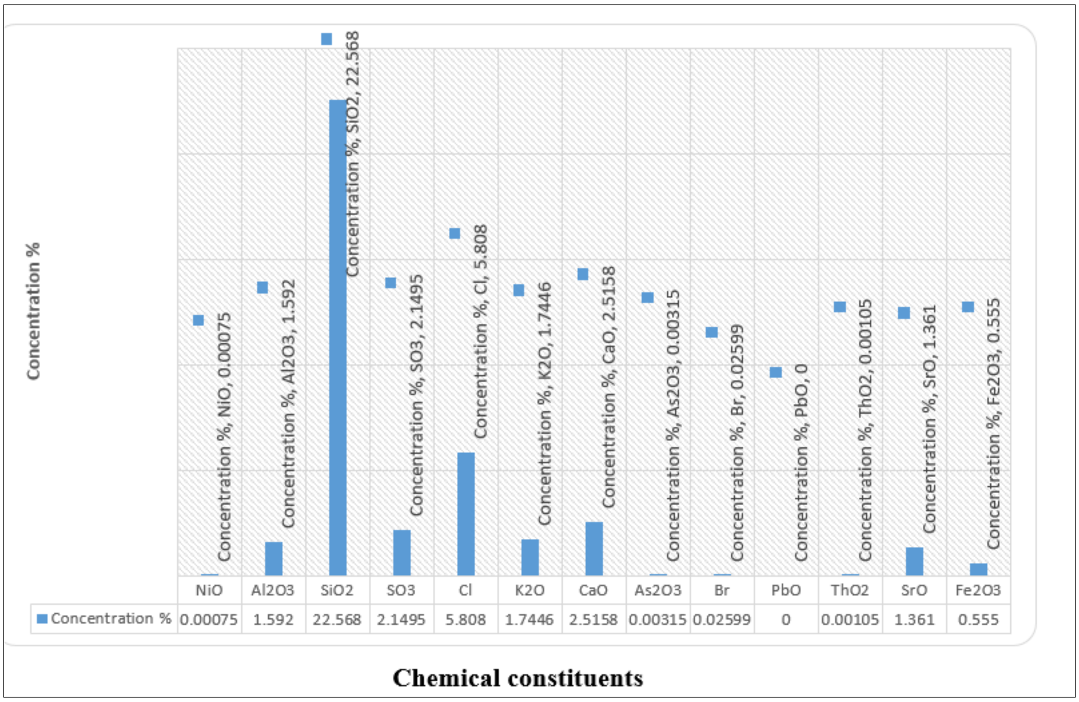

Figure 2 Inorganic chemical constituents of trona (Akanwu)

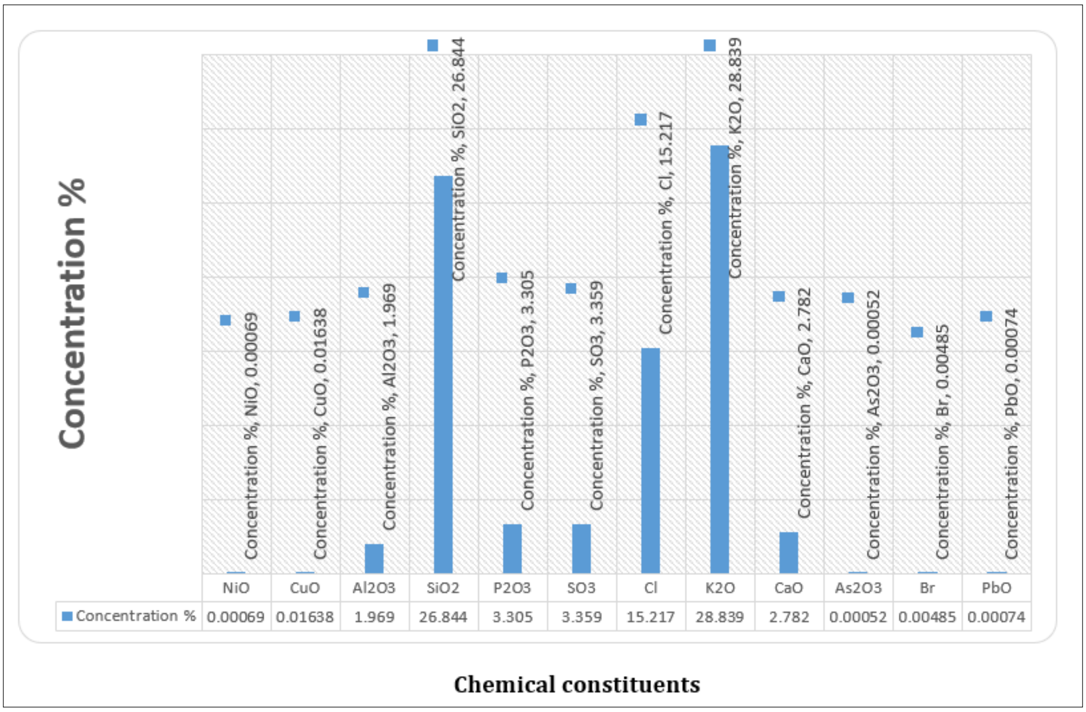

Figure 3 Inorganic chemical constituents of palm ash (Ngu)

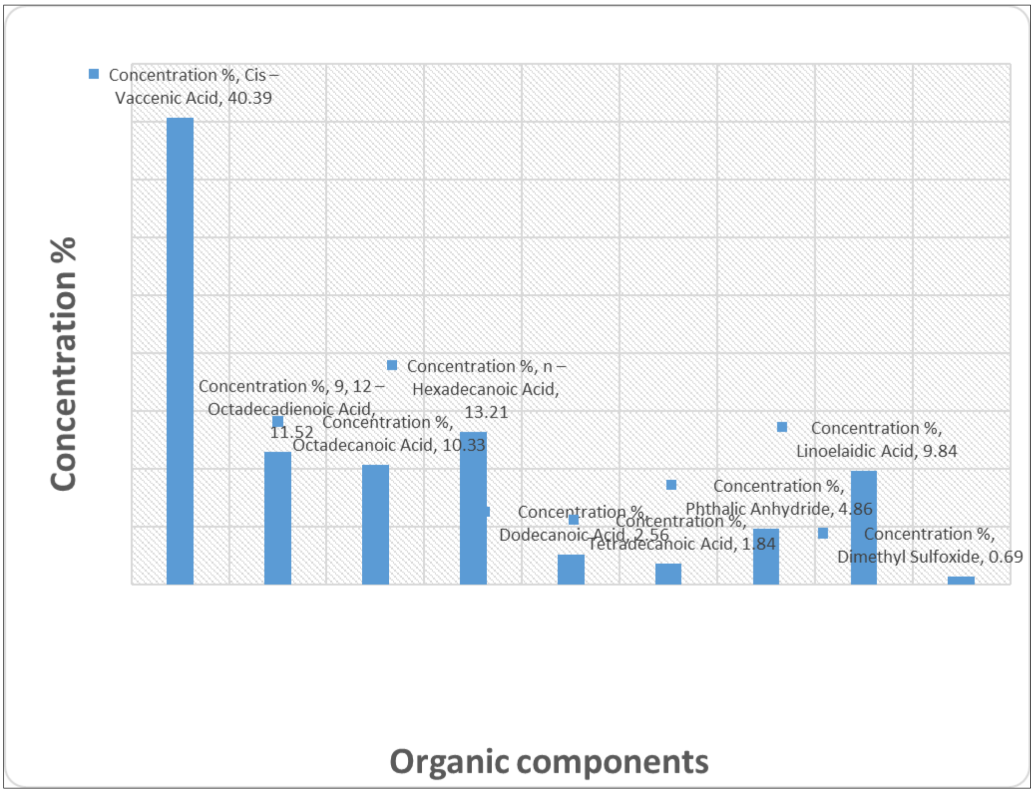

Figure 4 Organic chemical constituents of Alum

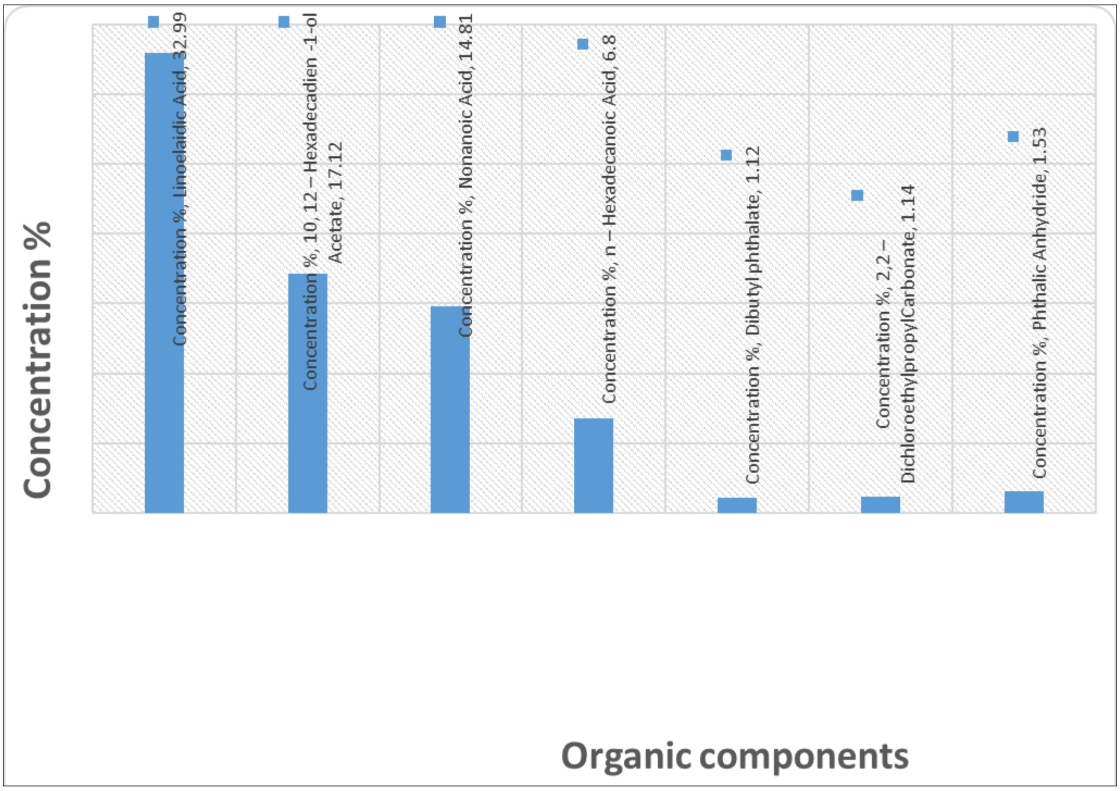

Figure 5 Organic chemical constituents of trona (Akanwu)

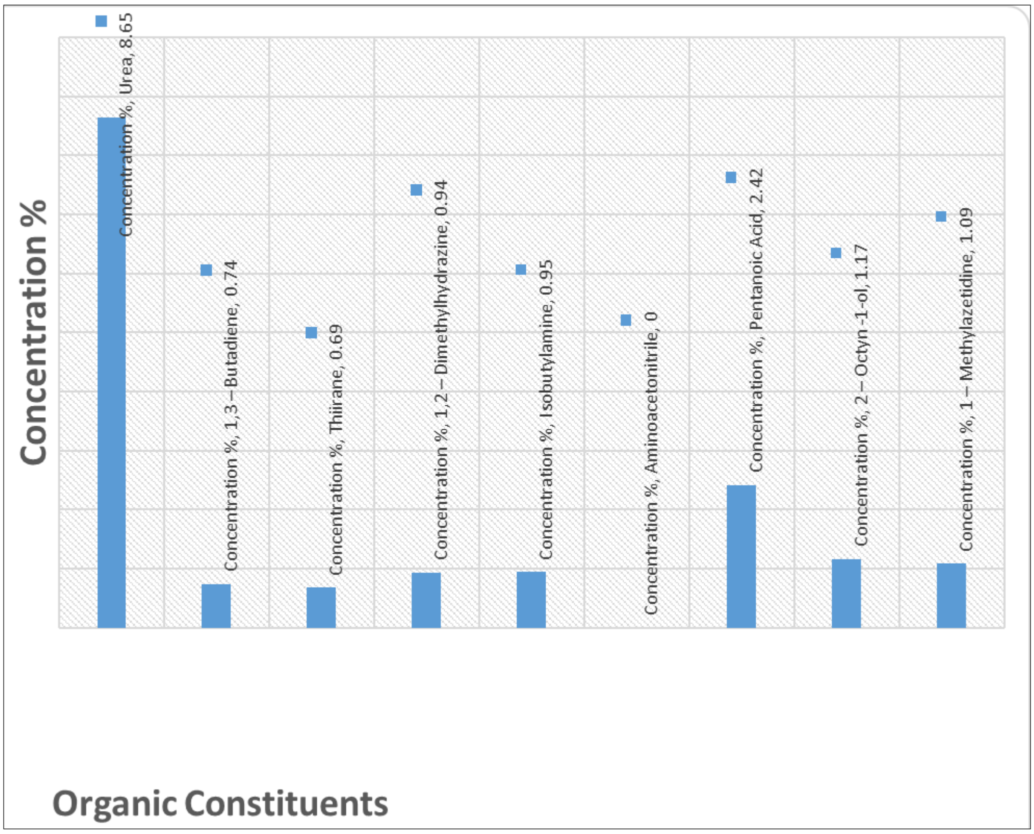

Figure 6 Organic chemical constituents of palm ash (Ngu)

4. Discussion

Drug discovery is a chronological process which is intended to identify a chemical agent or biomolecule for comprehensive evaluation as a potential drug. This study revealed that alum, trona and palm ash posses varying levels of potency against *Candida* isolates. Alum gave the best activity as observed in its MIC and MFC values. The MIC values include 50 mg/ml (*Candida albicans*), 25 mg/ml (*C. tropicalis*), 12.50 mg/ml (*C. glabrata*) and 12.50 mg/ml (*C. parapsilosis*), Ketoconazole (12.50 mg/ml – 50 mg/ml); while the MFC values were 50 mg/ml (*Candida albicans*), 50 mg/ml (*C. tropicalis*), 12.50 mg/ml (*C. glabrata*) and 25 mg/ml (*C. parapsilosis*), Ketoconazole (25 mg/ml – 50 mg/ml) as shown in tables 1 to 8. The high sulphur content must have contributed to this activity.Alum comprises oxides of sulphur (44.5 %), aluminium (14.49 %) etc. The heavy metals include oxides of lead, arsenic, nickel, accounting for <0.0010 % (very negligible) as shown in figure 1. The safety of alum as shown above was also reported by Brahmachari *et al.* (2019) who stated that notable advantages for the use of alum include cost effectiveness, availability, non-toxicity, reusability and ecofriendliness. The organic components include naturally occurring fatty acids (vaccenic acid, decanoic acid and linoelaidic acid) (figure 4) which exhibit some level of antimicrobial activity. These must have contributed to the antimicrobial efficacy of alum. The findings agreed with Ali *et al.* (2017), who pointed out that the potency of alum as an antimicrobial agent had been visibly demonstrated over the years through myriads of its beneficial activities and relevance in a broad spectrum of human research and development.

Ntukidem *et al.* (2002) reported that trona exhibited antimicrobial activity against pathogenic bacteria and fungi organisms including *Pseudomonas aeruginosa, Proteus spp, Candida albicans and C. pseudotropicalis.* The MIC values of trona against the isolates were 100 mg/ml (*Candida albicans*), 50 mg/ml (*C. tropicalis*), 6.25 mg/ml (*C. glabrata*) and 6.25 mg/ml (*C. parapsilosis*); while the MFC values were 100 mg/ml (*C. albicans*), 100 mg/ml (*C. tropicalis*), 12.50 mg/ml (*C. glabrata*) and 25 mg/ml (*C. parapsilosis*) as shown in tables 1 to 8. The inorganic components found in trona as shown in figure 2 include sulphur (2.14 %), chlorine (5.8 %), and potassium (1.7 %) while the heavy metals include lead (0 %), arsenic and nickel (<0.003 %). Sulphur and chlorine which are notable antimicrobials agents must have contributed immensely to the antimicrobial efficacy of trona. The organic components include linoelaidic acid, nonanoic acid and decanoic acid (figure 5). These organic fatty acids exhibit some level of antimicrobial properties. Parenteral use of trona is relatively safe while its topical application is considered very safe as shown in the findings.

Figure 3 showed the inorganic components of palm ash including potassium (28.8 %), sulphur (3.4 %), calcium (2.8 %), chlorine (15 %) etc while the average concentration of toxic heavy metals is <0.0007 %. The organic components were urea and fatty acids as shown in figure 6. Urea preparation (40 %) may also be used for non-surgical debridement of nails. It dissolves the intercellular matrix (Nicolaou and Montagnon, 2008). Urea and its derivatives have been reported by Patil *et al*. (2019) to exhibit some level of antimicrobial activity. Thus, the antimicrobial activity of palm ash as seen in the MIC and MFC values, is possibly due to sulphur, chlorine, urea and the fatty acids. The MIC values of palm ash were 100mg/ml against all the isolates; while the MFC values were 100 mg/ml (*Candida albicans*), 200 mg/ml (*C. tropicalis*), 100mg/ml (*C. glabrata*) and 200 mg/ml (*C. parapsilosis*) as shown in tables 1 to 8.

5. Conclusions

The findings have established that natural compounds such as trona, alum and palm ash are effective and safe antifungal agents *in vitro*; thus, could serve as potential raw materials in antifungal drugs production.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflicts of interest.

References

[1] Ali, A. H. and Zaigham, M. S. (2017). Alum a unique drug and its utilization in Unani medicine: A physicochemical and pharmacological review. International Journal of Research in Ayurveda Pharmacology, 8(2):17-22.

[2] Amadi, L. (2020). A Review of Antimicrobial Properties of Alum and Sundry Applications. Acta Scientific Microbiology, 3(4): 109 – 117.

[3] Austin, G. T. (1984). Shreve's Chemical process industries (5th ed.). New York, NY: McGraw-Hill. Page 357.

[4] Bongomin, F., Gago, S., Oladele, R. O. and Denning, D. W. (2017). Global and multi-national prevalence of fungal diseases-estimate precision. Journal of Fungi, 3:57.

[5] Brahmachari, G. (2019). Alum (KAl (SO4)2.12H2O) - An Eco- friendly and Versatile Acid-catalyst in Organic Transformations: A Recent Update. Current Green Chemistry, 6(1): 12-31.

[6] Bulatovic, S. M. (2015). Flotation of Industrial Minerals. Handbook of Flotation Reagents: Chemistry, Theory and Practice, 3: 153 – 162.

[7] Buss, A. D. and Butler, M. S. (2010). Natural product chemistry for drug discovery. The Royal Society of Chemistry, Cambridge. Page 153.

[8] Cheesbrough, M. (2018). Laboratory Practice in tropical Countries (2nd edition) Part 2. Cambridge University Press, Cambridge, United Kingdom.

[9] Civitello, L. (2017). Baking powder wars: the cutthroat food fight that revolutionized cooking. Urbana, Illinois: University of Illinois Press. Pp. 18–22.

[10] da Costa, J. P., Cova, M., Ferreira, R. and Vitorino, R. (2015). Antimicrobial peptides: an alternative for innovative medicines? Applied Microbiology and Biotechnology 99: 2023–2040.

[11] Dini, J. R. and Jones, R.W. (1998). Proceedings of the First International Soda Ash Conference: Geological Survey of Wyoming Public Information Circular 39, 2v.

[12] Fisher, M. C., Hawkins, N. J., Sanglard, D. and Gurr, S. J. (2018). Worldwide emergence of resistance to antifungal drugs challenges human health and food security. Science 360: 739–742.

[13] Hamill, R. J. (2013) Amphotericin B formulations: a comparative review of efficacy and Toxicity. Drugs, 73: 919 – 934.

[14] Kamka-Evans, C. I., Ngumah, M. O., Nwachukwu, C. U. and Ugochukwu, N. (2013). Comparative evaluation of phychochemical and antimicrobial activities of *Elaeis guineensis* tusks, Musa paradisiaca peels and potassium carbonate in bacterial isolate from fermented *Pentaclethra macrophylla* seeds. Journal of Global Biosciences, 2(1): 17 - 19.

[15] Li, G., Zhao, X., Wu, S., Hua, H., Wang, Q. and Zhang, Z. (2017). Dietary exposure to aluminium in the popular Chinese fried bread youtiao. Food Additives & Contaminants. Part A, Chemistry, Analysis, Control, Exposure & Risk Assessment, 34 (6): 972–979.

[16] McGinnis, M. R. (1980). Laboratory Handbook of Medical Mycology. New York: Academic Press.

[17] Nicolaou, K. C. and Montagnon, T. (2008). Molecules That Changed The World. Wiley-VCH. Page 11.

[18] Ntukidem, V. E., EtokAkpan, O., Abraham, N. A. and Umohinyang, E. U. (2020). Physicochemical and Antimicrobial Evaluations of Food Grade Ash Aqueous Physicochemical and Antimicrobial Evaluations of Food Grade Ash Aqueous extract from Furnace and Charred Plantain Peel and Palm Bunches : A Comparative Approach. International Journal of Food and Nutrition Sciences, 5: 83–90.

[19] Odds, F. C., Arai, T., DiSalvo, A. F., Evans, E. G. V., Hay, R. J., Randhawa, H. S., Rinaldi, M. G. and Walsh, T. J. (1992). Nomenclature of fungal diseases. Journal of Medical Veterinary Mycology, 30:1.

[20] Okoye, J., Oranefo, N. and Okoli, A. (2016). Comparative Evaluation of the Effects of Palm Bunch Ash and Trona on the Liver of Albino Rats. African Journal of Cellular Pathology, 6: 21–27.

[21] Patil, M., Noonikara-Poyil, A., Joshi, S. D., Patil, S. A., Patil, S. A. and Bugarin, A. (2019). New Urea Derivatives as Potential Antimicrobial Agents: Synthesis, Biological Evaluation, and Molecular Docking Studies. Antibiotics, 8(4): 178.

[22] Patridge, E., Gareiss,P., Kinch,M. S. and Hoyer, D.(2016). An analysis of FDA-approved drugs: Natural products and their derivatives. Drug Discovery Today, 21(2): 204–207.

[23] Rabiu, A. and Malami, S. (2019). Toxicity Study of Potash Extract, "jar Kanwa": An earthy materialconsumed for Remedy of various Ailments in Northern Nigeria. Journal of biomedical research and clinical practice, 2(4): 197 – 201.

[24] Rice, J. K. (1957). The use of organic flocculants and flocculating aids in the treatment of industrial water and industrial waste water. Symposium on Industrial Water and Industrial Waste Water, 207: 41–51.

[25] Roemer, T. and Krysan, D. J. Antifungal Drug Development: Challenges, Unmet Clinical Needs, and New Approaches. Cold Spring Harbour Perspective Medicine, 4:a019703.

[26] Udemezue, O. I. and Oyeka, C. A. (2021). Antifungal potency of potash compounds against *Candida* species isolated from high vaginal swabs of women attending a teaching hospital in Nigeria. European Journal of Biomedical and Pharmaceutical sciences, 8(4): 330 – 334.

[27] Vignesh, K., Niresh, S. J., Saravanasingh, K. and Uma, A. P. (2019). Padikaram (alum)–a unique drug and its utilization in Siddha medicine: a pharmacological review. Siddha Papers, 14(2):1-2.

[28] Walsh, T. J., Gonzalez, C., Lyman, C. A., Chanock, S. and Pizzo, P. A. (1995). Invasive fungal infections in children: recent advances in diagnosis and treatment. Advances in Pediatrics Infectious Diseases, 11:175.