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Synthesis of Flavonoids Derivatives using Polar and Non-Polar Extract of Red Onion Skin (*Quercetin*) with Cashew Nut Shell Liquid

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ABSTRACT: Red Onion skin extract and Cashew nut shell liquid has been considered as one of the best antioxidant and anti-inflammatory precursors, as it contains various polyphenols and important flavonoids. In this research, flavonoid derivatives were successfully synthesized from polar and non-polar extract of red onion skin, non-polar extract of cashew nut shell liquid and a combination of the onion skin extracts and cashew nut shell liquid. In this process, crude red onion skin extract was obtained using potassium carbonate via maceration process and acetone via soxhlet extraction. Cashew nut shell liquid was extracted using acetone via soxhlet extraction. The synthesis was carried out via the Williams ether synthesis using 1,2-dibromoethane in the presence of a base catalyst. FTIR of the products confirmed its modification. From the result, it can be concluded that the non-polar extract performed better than the polar extract. Hence for further studies, non-polar solvents should be considered for extraction.

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Flavonoids are a subset of polyphenols with a wide range of properties. Because there are over 3000 distinct flavonoids, there are differences in their location, structure, and synthesis. Flavonoids can be found in a variety of plant tissues such as flowers, fruit, foliage, heartwood, and bark. The flavan rings are labeled A, C, and B, with a systematic numbering of carbon atoms (Ravan, 1999). The presence of numerous phenol groups dominates the chemistry of flavonoids. As a result, common reactions include acid and base catalyzed rearrangements, nucleophilic substitution, and electrophilic aromatic substitution. The phenol groups also give flavonoids their strong complexing and antioxidant activities. (McGraw, 1989). Red onions, also known as purple onions in some European nations, are an onion plant variation with purplish-crimson skin and white meat tinted with red. The onion, Allium cepa L., is a member of the Lilliaceae family, popularly known as the lily family. It is cultivated all over the world. They are the second most popular horticultural vegetable after tomatoes (bulb vegetable to be precise). Griffiths and colleagues (Griffiths *et al.*, 2002). On the other hand, Cashew Nut Shell Liquid (CNSL) is a by-product of the cashew nut business that is extracted from the spongy mesocarp of the cashew nut (Anacardium occidentale L.) shell using a variety of processes, the most common of which involves solvent extraction (Gandhi *et al.*, 2012). It contains phenolic lipids such as anacardic acid, cardol, cardanol, and 2-methyl cardol in abundance. Hence the objective of this paper is to synthesize flavonoid derivatives using polar and non-polar extract of red onion skin (quercetin) with cashew nut shell liquid.

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MATERIALS AND METHOD

Red Onion Skin: Choba Market in Port Harcourt, Rivers State, provided the red onion skin. To clean it up and make it acceptable for mixing, the red onion skin was hand-picked and sun-dried for a few days. A blender was used to expand the surface area of the red onion skin. This is done to boost the rate of extraction by enhancing the interaction between the rose and the solvent. The blended red onion skin was packed in the Soxhlet extractor thimble with a Whatman filter paper and extracted by refluxing with acetone at 60-70°C until the solvent became clear in the thimble. Distillation was used to separate the extract from the solvent.

Cashew Nut Shell Liquid (CNSL): Whole cashew nuts (CN) were purchased from Ihube village in Imo State, Nigeria's Okigwe Local Government Area. To remove contaminants, the cashew nut was washed and sun dried for a few days before being chopped lengthwise, dekernelled, and crushed in a hydraulic press (to increase the surface area for extraction). The liquid from the cashew nut shell was removed in the same way as the red onion peel.

Chemicals: Industrial grade acetone, 1, 2-dibromoethane, and potassium carbonate are among the compounds used (Analar grade Aldrich Chemicals). Without additional purification, all compounds were utilized as received.

Williams Ether Synthesis: The acid-catalyzed dehydration of alcohols is a simple way to get ethers. This is confined to symmetric ethers derived from primary alcohols, such as diethyl ether produced industrially from ethanol. For the creation of more complex ethers, the Williamson ether synthesis is superior. As demonstrated below, an alkoxide interacts with an alkyl halide in an SN2 type reaction (McMurry, 1999).

$$RO + R'X \longrightarrow ROR' + X$$

Alcohols and phenols can both be used in the reaction. Alcohols react with sodium to generate an alkoxide, which is then subjected to halide treatment. Because phenols are more acidic, a base like sodium hydroxide or potassium carbonate is sufficient to produce the alkoxide (Smith, 2001). C-alkylation is a common side reaction for phenols, however it can be reduced by using a polar aprotic solvent rather than a protic solvent. This is due to the solvent's capacity to form a strong hydrogen bond with the phenoxide oxygen, reducing its ability to act as a nucleophile. As a result, the phenoxide's ortho and para carbon atoms can fight for nucleophilic displacement (Feuer, 1967). Because alkyl bromides are more reactive than alkyl chlorides and less prone to dehydrohalogenation than alkyl iodides, they produce higher yields. Because the reaction is catalyzed by an SN2 mechanism, primary alkyl halides are the optimum choice because secondary substrates can result in E2 elimination. Unsymmetrical ethers should therefore be made by reacting a more hindered alkoxide with a less hindered halide (McMurry, 1999). Because ethers have a low reactivity, they are commonly used as solvents. There are just a few processes that they go through, one of which is acidic cleavage. To cleave the ether bonds, a strong acid and high temperatures are necessary. Because of their inertness, cyclic ethers are utilized as solvents in the same way that open chain ethers are. Epoxides or oxiranes, which are three-membered ring ethers, are far more reactive (McMurry, 1999).

Etherification of acetone extract of red onion skin (quercetin) with 1, 2 – dibromoethane in acetone by the Williamson Ether Synthesis: In acetone, quercetin (approx. 1 g, 0.003 mol) was dissolved (30 mL). The mixture was heated under reflux for 15 minutes with an addition of excess of finely crushed potassium carbonate (approx. 0.5g, 0.004mol) and then allowed to cool. After adding 1, 2-dibromoethane (0.3ml), the mixture was refluxed for 24 hours. The reaction mixture was neutralized with HCl (0.1 molL-1) and concentrated by rotary evaporation to obtain a brown solid that was water soluble but not acetone soluble. Filtration was used to remove the solid phase. The solution was acidified with HCl (0.1 molL-1) and rotary evaporation was used to concentrate it (Johnstone, 1979). The reaction product was accessed via FTIR.

Esterification of cashew nut shell liquid with 1, 2 – dibromoethane by the Williamson Ether Synthesis: Adding potassium carbonate (approx. 0.5g, 0.004mol) to (10ml) cashew nut shell liquid and refluxing for 15 minutes was used to prepare the product with 1,2-dibromoethane product. Allowing the responding vessel to cool was necessary. (1.2ml) 1,2-dibromoethane was added and the mixture was refluxed for one hour. The reaction mixture was neutralized with HCl (0.1 mol/L) and concentrated by rotary evaporation to obtain a crimson liquid. The functional group contained in the product was confirmed using FTIR (Hashida, 2002).

Etherification and esterification of a mixture of cashew nut shell liquid and acetone extract of red onion skin (quercetin) with 1, 2 – dibromoethane by the Williamson Ether Synthesis: Quercetin (approx. 8.7 g, 0.029 mol) and powdered potassium carbonate (approx. 0.5g, 0.004mol) were dissolved in cashew nut shell liquid (10mL). The solution was heated to reflux for 15 minutes, then cooled before adding 1,2 dibromoethane (1.2ml). The reaction mixture was refluxed for 1 hour, then cooled, filtered, and concentrated by rotary evaporation to produce a brown liquid (Pizzi, 1983). The functional group contained in the molecule was confirmed using FTIR.

Etherification of potassium carbonate extract of red onion skin (quercetin) with 1, 2 – dibromoethane in acetone by the Williamson Ether Synthesis: (approx.1 g, 0.003 mol) Quercetin was dissolved in water (20 mL). The mixture was heated under reflux for 15 minutes and then allowed to cool with an excess of finely crushed potassium carbonate (approx. 0.5g, 0.004mol). After adding 1, 2-dibromoethane (1.2ml), the mixture was refluxed for 1 hour. The reaction mixture was neutralized with HCl (0.1 molL-1) and concentrated by rotary evaporation to obtain a brown solid that was water soluble but not acetone soluble. Filtration was used to remove the solid phase. The solution was acidified with HCl (0.1 molL-1) and rotary evaporation was used to concentrate it (Johnstone, 1979). The reaction product was accessed via FTIR.

Etherification and esterification of a mixture of cashew nut shell liquid and potassium carbonate extract of red onion skin (quercetin) with 1, 2 – dibromoethane by the Williamson Ether Synthesis: Quercetin (approx. 8.7 g, 0.029 mol) and powdered potassium carbonate (approx. 0.5g, 0.004mol) were dissolved in cashew nut shell liquid (10mL). The solution was heated to reflux for 15 minutes, and then cooled before adding 1,2- dibromoethane (1.2 mL). The reaction mixture was refluxed for 1 hour, then cooled, filtered, and concentrated by rotary evaporation to produce a brown liquid (Pizzi, 1983). The functional group contained in the molecule was confirmed using FTIR.

RESULTS AND DISCUSSION

The Williamson ether synthesis, in which an alkoxide is combined with an alkyl halide, was used to try to make polyphenol ethers. The corresponding polyphenol ethers were produced by reacting quercetin, cashew nut shell liquid, and a combination of the two with 1,2 –dibromoethane. Initially, quercetin was employed to determine the best response conditions.

Table 1: Physicochemical properties of flavonoid derivatives

Compound code	Reactants	Reaction temperature	Reaction time (hour)	Appearance
P1	Acetone extract (quercetin) + 1,2-dibromoethane	Reflux	24	Brown solid
P2	Cashew nut shell liquid + 1,2-dibromoethane	Reflux	1	Red liquid
P3	Acetone extract (quercetin) + cashew nut shell liquid + 1,2-dibromoethane	Reflux	1	Brown liquid
P4	Potassium carbonate extract (quercetin) + 1,2-dibromoethane	Reflux	1	Brown solid
P5	Potassium carbonate extract (quercetin) + cashew nut shell liquid + 1,2-dibromoethane	Reflux	1	Brown liquid

Following that, these desired reaction conditions were used to react cashew nut shell liquid. Potassium carbonate is a common base for such a reaction, according to Wurm and Rehn (1985).

The use of dipolar aprotic solvents has been demonstrated to favor this SN2 reaction (Wurm and Rehn, 1985; Babu *et al.*, 2005; Hoelldampf, 2007), but the reaction can also take place in water (Wurm and Rehn, 1985; Babu *et al.*, 2005; Hoelldampf, 2007). (Mitchell *et al.*, 1998). P1 through P5 were allocated to the substances that were synthesized. The compounds synthesized were analyzed using FTIR as earlier stated.

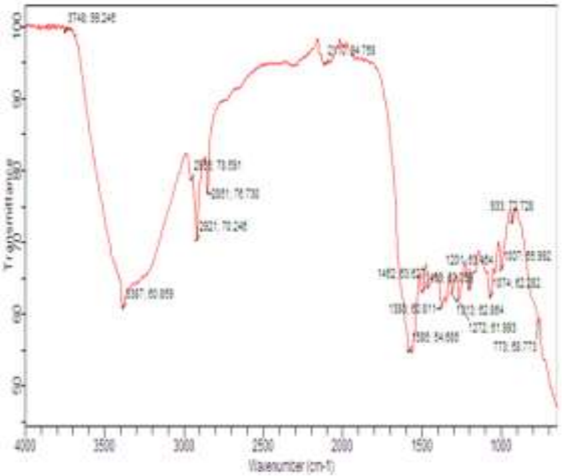

Fig 1: FTIR Spectrum for P1

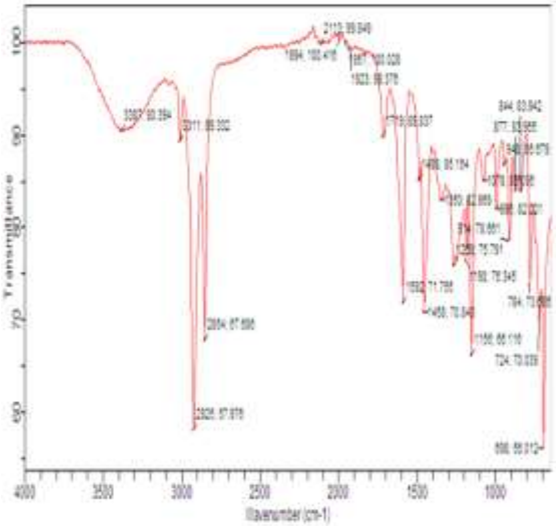

Fig 2. FTIR Spectrum for P2

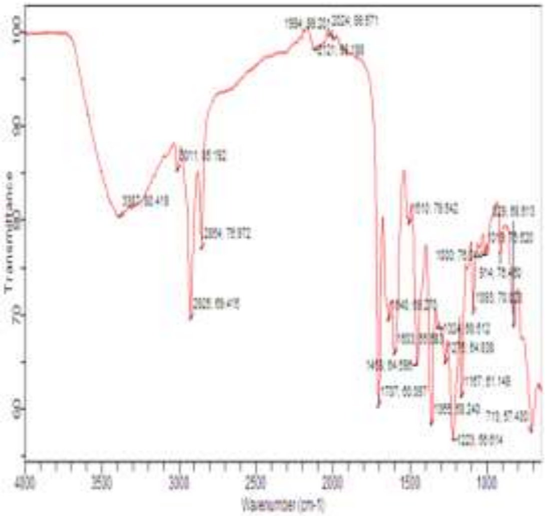

Fig 3. FTIR Spectrum for P3

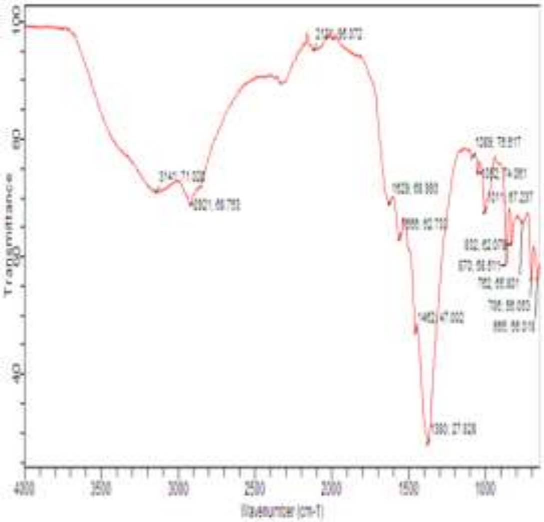

Fig 4. FTIR Spectrum for P4

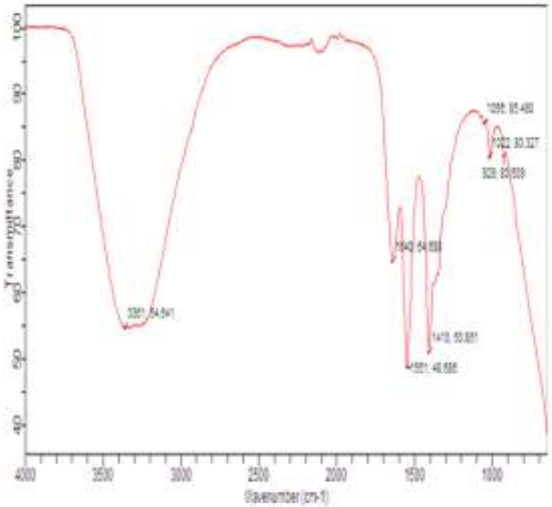

Fig 5. FTIR Spectrum for P5

P1's FTIR spectrum, as seen in its spectra in Fig. 1, has distinct peaks that correspond to the functional groups in Quercetin. The phenol group's O-H vibration produces a strong and broad absorption band at 3387 cm-1. The C–H stretching vibration of alkene groups occurs at 2921 cm-1, while the C–H vibrations of methylene and methyl groups of the meta substituted hydrocarbon chain occur at 2855 cm-1 and 2851 cm-1, respectively. At 1283 cm-1, the acid C=O linked to the aromatic ring absorbs, whereas the acid C–O stretching vibration is at 1201 cm-1. C=C stretching vibrations in alkenes occur at 2110 cm-1, while C=C aromatic stretching vibrations occur at 1585 cm-1. Methyl C–H deformation vibrations occur at 1462.9 cm-1 and 933 cm-1, while the alkene C–H deformation vibration occurs at 773 cm-1. In the case of P2, the FTIR spectrum shows distinctive peaks corresponding to the functional group in anarcadic acid, as shown in Fig 2. The O-H vibration of the phenol group coincides with that of carboxylic acid, resulting in a strong and broad absorption band at 3387 cm-1. Other absorption bands found at 3011 cm-1, 2925 cm-1, 2854 cm-1, and 1699.7 cm-1 add to the peaks interpreted in P1. Alkene C=C stretching vibrations, on the other hand, occur at 1592 cm-1, while aromatic C=C vibrations occur at 1458.7 cm-1. At 1488 cm-1 and 1350 cm-1, methyl C–H deformation vibrations occur; an absorption band at 1190 cm-1 corresponds to ester C–O stretching vibration, while the band at 724 cm-1 corresponds to alkene C–H deformation vibration. The FTIR spectra of P3 contain typical peaks corresponding to the functional group in quercetin and anarcadic acid, as shown in fig. 3. The O-H vibration of the phenol group coincides with that of carboxylic acid, resulting in a strong and broad absorption band at 3387 cm-1. The disappearance of the band at 1699.7 cm-1 indicates that the acid group is involved in the creation of ester bonds. Other absorption bands seen at 3011.7 cm-1, 2922.2 cm-1, and 2855.1 cm-1 have already been attributed to P1, while those seen at 1510 cm-1, 1458 cm-1, 1365 cm-1, 1324 cm-1, 1275.0 cm-1, and 713.0 cm-1 have already been attributed to P2. The bands exhibited in fig 3.4-3.5 for P4 and P5 are much weaker and fewer. For P1 and P2, the visible bands have previously been deciphered.

Conclusion: From the study, the following conclusions can be deduced: The quercetin acetone extract performed better than the potassium carbonate extract. Polyphenols' hydrophobicity was shown to be increased as a result of the reaction. The etherification of polyphenols, particularly quercetin, has been found to alter the material's physical properties. Etherification of polyphenols was a new way to change their chemical and physical properties.

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