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In Silico Identification of Protein Targets for Drug-like Compounds from Epicarp Extract of *Cola rostrata* K. Shum

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ABSTRACT: Fruit epicarp has been found to contain several bioactive compounds which are useful for herbal treatment of several ailments and diseases. The phytochemicals present in *C. rostrata* epicarp as well as their potential to bind to human proteins and modify their function have not been investigated. This study, therefore, identified the top protein targets of drug-like components of *C. rostrata* epicarp extract in humans as well as the disease conditions associated with the targets. The identities of constituents of methanol and n-hexane fractions of absolute ethanol extract of *C. rostrata* epicarp were determined via GCMS analysis. Druglikeness (adherence to Lipinski, Ghose, Veber, Egan, and Muegge filters) and the protein targets of drug-like constituents were determined using SwissADME and SwissTargetPrediction web tools. GCMS analyses revealed the presence of 49 compounds in the n-hexane and methanol fractions. Corynan-16-carboxylic acid, 16,17-didehydro-9,17-dimethoxy-, methyl ester, (16E)-, a yohimbine derivative, was abundant (13.33%) in the methanol fraction. The n-hexane fraction was rich in odd-chain fatty acids and phytosterols. Four drug-like compounds were identified in the fractions: **(1)** Azelaic acid, monoethyl ester; **(2)** 3-(2-Methoxymethoxyethylidene)-2,2 dimethylbicyclo[2.2.1]heptane; **(3)** Cyclododecanol, 1-aminomethyl-, and **(4)** Corynan-16-carboxylic acid, 16,17-didehydro-9,17-dimethoxy-, methyl ester, (16E)-. The predicted top protein targets of the drug-like compounds include carbonic anhydrase II, protein-tyrosine phosphatase 1B, sphingosine kinase 1, maltase-glucoamylase, adenosine A2b receptor, P2X purinoceptor 7, MAP kinase p38 alpha, δ-opioid receptor, and alpha-2 adrenergic receptors. Findings show that *C. rostrata* epicarp contains drug-like phytochemicals with potential against cancer, diabetes, pain and inflammatory diseases, and the extract could have aphrodisiac potential.

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The epicarp (fruit peel) is the epidermal layer that surrounds and protects the underlying mesocarp from microbial infection and water penetration, and at the same time it ensures gaseous exchanges with the external environment (Hansmann & Combrink, 2003). The epicarp of many tropical fruits is not edible and it constitutes a large mass of wasted plant materials each year. Recent studies have focused on turning fruit peels from constituting environmental nuisance to generating wealth and harnessing their rich phytochemical content for healthcare purposes (Torres-León *et al*., 2018; Veloso *et al*., 2020; Hikal *et al*., 2021; Osorio *et al*., 2021). Extracts from the epicarp of many tropical fruits have been reported to possess antimicrobial, antioxidant and other therapeutic potentials, which are useful in treating several disease conditions (Siombor & Anyam, 2015; Ibrahim *et al*., 2017; Albuquerque *et al*., 2020; Hikal *et al*., 2021). The fruit peel of Citrus species have been found to possess high antioxidant, anti-inflammatory and anti-nociceptive agents which could be used in pharmaceutical, nutraceutical or herbal preparations (Malleshappa *et al*., 2018; Ugbabe *et al*., 2019). The health benefits of banana peel and its extract was reported Kumar *et al* (2012); it was reported to contain some neurotransmitters: norepinephrine, dopamine,

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serotonin and fungicidal agents (Kumar *et al*., 2012). The knowledge of the constituents of extracts is useful in the matching bioactive component with biomolecular targets and indirectly, the kind of diseases the extract may be potent against. *In silico* protein target prediction and molecular docking have been used in the selection of potential drug-like components of natural products for chemical lead discovery against many ailments and diseases (Oduselu *et al*., 2019; Asghar *et al*., 2021; Oh *et al*., 2021). *Cola rostrata* is an underutilized and uncultivated tree crop that produces crunchy tasty edible fruits; the plant belongs to the sub-family Sterculiaceae and it is one of the Cola species that are commonly called Monkey kola (Odion *et al*., 2013). Extracts of *C. rostrata* epicarp were reported to contain polyphenols, tannins, and antimetabolites such as hydrocyanic acid, phytic acid and oxalic acids; it also possess antimicrobial activity (Ebana *et al*., 2015). The identification of the drug-like compounds present in *C. rostrata* fruit epicarp as well as the determination of their protein targets in humans have not be done. *In silico* fishing and molecular docking studies of phytochemicals from fruit epicarp will fast-track the isolation of compounds that can be eventually developed into drugs for various diseases and will thus stop wastage of valuable fruit materials. Hence, the objective of this study is to investigate the in-silico identification of protein targets for drug-like compounds from ethanol extract of the epicarp of *Cola rostrata* K. Shum

MATERIALS AND METHODS

Fruit collection and Authentication: C. rostrata fruit is enjoyed by the people of the South-east and South-south regions of Nigeria; the yellow mesocarp is eaten fresh while the epicarp and seed are thrown away (Plate 1). Ripe fruits of *C. rostrata* were collected fresh from trees at Utu Ikot–Essien, Ikot Ekpene Local Government Area of Akwa-Ibom State, Nigeria, and authenticated by Professor Abiodun Ayodele of the Department of Botany, University of Ibadan.

Preparation of Extract: The epicarp was separated from other parts of the fruit, cut into small pieces, and air-dried under shade at ambient room temperature for four months. The dried epicarp was pulverized using a blender and soaked in absolute ethanol for six days with regular rigorous shaking of the extraction vessel to disperse more phytochemicals. The mixture was filtered, and the filtrate was concentrated using the rotary evaporator at 45 ºC and air-dried in the fume cupboard. Using the separatory funnel, the solid extract was partitioned between 70% methanol solution and n-hexane (3:2) into epicarp polar fraction and non-polar fraction.

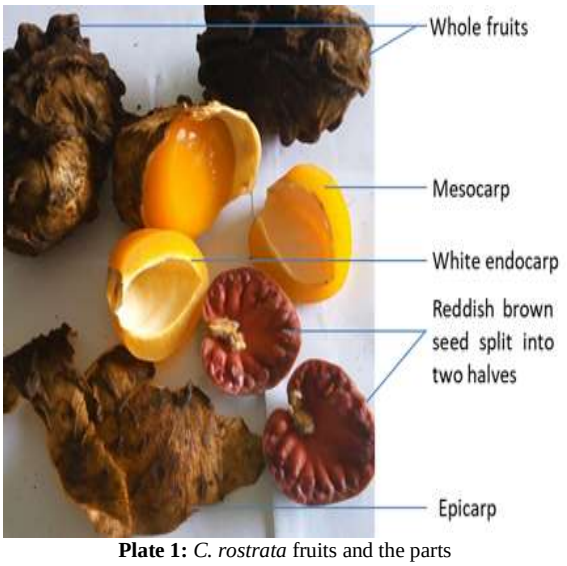

Plate 1: *C. rostrata* fruits and the parts

GCMS Analysis of Fractions: The fractions were analyzed on Gas Chromatography (Agilent Technologies, 7890, USA) Apparatus coupled with a Mass Spectroscope (Agilent Technologies, 5975, USA). The column (Agilent Technologies, HP5MS) had a length of 30 cm, internal diameter of 0.320 mm and thickness of 0.25 µm. The initial oven temperature was set to 80 ºC for 2 min, increased at a rate of 12 ºC per min to 240 ºC and then held for 6 min. The volume injected was 1 µl and the mode of analysis was splitless. The interface temperature between the Gas Chromatography apparatus and the Mass Spectroscope was 250 ºC. The total run time was 22 min and scans ranged from 50 to 500 m/z, and a search of the NIST14 library was used to identify the compounds represented by the peaks.

Drug-likeness and Identification of Protein Targets of Components of Extract Fractions: For each of the compounds identified via GCMS with purity score above 50%, the corresponding simplified molecular-input line-entry system (SMILES) notations were obtained from PubChem (https://pubchem.ncbi.nlm.nih.gov). Using the SMILES, the pharmacokinetic properties (absorption, distribution, metabolism and excretion) of each of the compounds were determined *in silico* as a way of determining their drug-likeness on SwissADME (www.swissadme.ch). The compounds which did not show violation of Lipinski's rule of five and Ghose, Veber, Egan and Muegge filters were selected for protein target prediction on SwissTargetPrediction (www.swissadme.ch) with "Homo sapiens" selection. The top seven protein targets obtained for each drug-like compound were selected and the importance of

their inhibition to the management of diseases was considered.

RESULTS AND DISCUSSION

GCMS Identification: The GCMS analysis of the non-polar fraction of *C. rostrata* ethanol epicarp extract revealed the presence of 29 compounds with retention times ranging from 9.842 min to 21.696 min (Table 1). The common constituents are fatty acids, fatty acid esters and phytosterols. The fatty acids include those with odd carbon numbers in their chain: pentadecanoic acid and heptadecanoic acid. n-hexadecanoic acid is the most abundant constituent in the fraction, which had a proportion of 27.45% in the fraction, followed by ethyl 9.cis.,11.trans.-octadecadienoate, which had a proportion of 12.09%.

Table 1: Constituents of non-polar fraction of *C. rostrata* epicarp extract as revealed by GCMS.

	Constituents	RT(min)	Area%	MM(g/mol)
1	3-Cyclopentylpropionic acid, ethyl ester	9.842	0.60	170.25
2	Azelaic acid, monoethyl ester	11.764	1.20	216.27
3	Tetradecanoic acid	12.819	0.67	228.37
4	Pentadecanoic acid	13.830	1.19	242.39
5	Hexadecanoic acid, methyl ester	14.408	0.80	270.45
6	n-Hexadecanoic acid	15.030	27.45	256.42
7	Hexadecanoic acid, ethyl ester	15.096	6.59	284.48
8	cis-9-Tetradecenoic acid, propyl ester	15.663	0.80	268.40
9	Heptadecanoic acid	15.807	1.69	270.50
10	Z,Z-10,12-Hexadecadien-1-ol acetate	16.519	0.66	280.44
11	Octadecanoic acid	16.752	7.09	284.48
12	Octadecanoic acid, ethyl ester	16.918	2.09	312.53
13	9,12-Octadecadienoic acid (Z,Z)-	17.230	0.76	280.44
14	Cyclohexene, 4-(4-ethylcyclohexyl)-1-pentyl-	17.441	1.68	262.50
15	7,10-Octadecadienoic acid, methyl ester	17.841	0.59	294.47
16	Z-8-Methyl-9-tetradecen-1-ol formate	18.029	0.86	268.43
17	9,12-Octadecadienoic acid (Z,Z)-	18.263	5.32	280.44
18	Ethyl 9.cis.,11.trans.-octadecadienoate	18.418	12.09	308.50
19	Naphthalene, decahydro-2-methyl-	18.685	2.28	152.27
20	2-Dodecen-1-yl(-)succinic anhydride	18.840	3.84	266.38
21	9-Tricosene, (Z)-	19.518	0.88	322.61
22	Stigmasta-4,22-diene	19.663	1.59	395.70
23	β-Sitosterol	19.763	2.69	414.71
24	Docosanoic acid	19.974	2.75	340.58
25	3-(2-Methoxymethoxyethylidene)-2,2 dimethylbicyclo[2.2.1]heptane	20.162	0.79	210.31
26	1-(4-Methoxyphenylazo)-2-phenoxynaphthalene	20.729	0.92	354.40
27	γ-Sitosterol	20.918	6.13	414.71
28	Stigmasterol	21.073	3.68	412.69
29	Stigmasta-4,22-diene	21.696	2.33	395.70

RT = retention time, MM = molecular mass

The GCMS analysis of the polar fraction of the epicarp extract revealed the presence of 22 compounds in the fraction, with retention times ranging from 14.408 min to 21.518 min (Table 2). The most abundant compound in the fraction was methanesulfonic acid (17-cyano-10,13-dimethylhexadecahydrocyclopenta[a]phenanthren-17-yl ester), which was 13.68% of the extract fraction. Corynan-16-carboxylic acid, 16,17-didehydro-9,17-dimethoxy-, methyl ester, (16E)- was the second in proportion with an area percent of 13.33%.

Druglikeness of Constituents: From both fractions, four compounds satisfied all the conditions of Lipinski, Veber, Egan, Ghose and Muegge filters: (1) Azelaic acid, monoethyl ester, (2) 3-(2-Methoxymethoxyethylidene)-2,2 dimethylbicyclo[2.2.1]heptane, (3) Cyclododecanol, 1-aminomethyl-, and (4) Corynan-16-carboxylic acid, 16,17-didehydro-9,17-dimethoxy-, methyl ester, (16E) (Fig. 1). Their solubility, bioavailability and pharmacokinetic properties are shown in Table 3. Two compounds failed to satisfy Muegge conditions for druglikeness but did not violate other filters; these two compounds violated only one condition each. These compounds are 2-Dodecen-1-yl(-)succinic anhydride (violation: XLOGP3 > 5) and 2(1H)-Naphthalenone, octahydro-4a-methyl-7-(1-methylethyl)-, (4a.alpha.,7.beta.,8a.beta.)- (violation: heteroatoms < 2). The two compounds have some properties in common: bioavailability score of 0.55, high gastrointestinal absorption, both are blood-brain barrier permeant, both are not substrates for P-glycoprotein, and they inhibit one or more members of

the cytochrome protein family members. The only difference between them is in the degrees of solubility in water, as 2-Dodecen-1-yl(-)succinic anhydride is only moderately soluble while 2(1H)-Naphthalenone, octahydro-4a-methyl-7-(1-methylethyl)-, (4a.alpha.,7.beta.,8a.beta.)- is soluble.

Table 2: Constituents of polar fraction of *C. rostrata* epicarp extract revealed by GCMS

	Constituents	RT(min)	Area%	MM(g/mol)
1	Hexadecanoic acid, methyl ester	14.408	1.48	270.45
2	n-Hexadecanoic acid	14.797	8.57	256.40
3	Bicyclo[2.2.2]octane, 2-methyl-	16.052	1.55	124.22
4	2-Myristynoyl-glycinamide	16.419	1.29	280.41
5	Oleic Acid	16.641	2.89	282.50
6	Methyl 9,12-heptadecadienoate	17.185	1.59	280.40
7	7-Pentadecyne	18.029	1.24	208.38
8	2(1H)-Naphthalenone, octahydro-4a-methyl-7-(1-methylethyl)-, (4a.alpha.,7.beta.,8a.beta.)-	18.241	2.23	208.34
9	2(1H)-Naphthalenone, octahydro-4a-methyl-7-(1-methylethyl)-, (4a.alpha.,7.beta.,8a.beta.)-	18.385	4.70	208.34
10	(3R,4aS,8aS)-8a-Methyl-5-methylene-3-(prop-1-en-2-yl)-1,2,3,4,4a,5,6,8a-octahydronaphthalene	18.674	4.96	202.33
11	13-Tetradece-11-yn-1-ol	18.840	5.34	208.34
12	Silicic acid, diethyl bis(trimethylsilyl) ester	19.107	2.28	296.58
13	2H-3,9a-Methano-1-benzoxepin, octahydro-2,2,5a,9-tetramethyl-, [3R-(3.alpha.,5a.alpha.,9.alpha.,9a.alpha.)]-	19.518	1.56	222.37
14	Cyclododecanol, 1-aminomethyl-	19.651	1.38	213.36
15	2-[1-(3,4-Dimethyl-phenyl)-1H-tetrazol-5-ylsulfanyl]-N-phenethyl-acetamide	19.874	3.66	367.50
16	2-Hydroxychalcone	20.029	1.76	224.25
17	4-Methoxy-6-methyl-5-nitroisobenzofuran-1,3-dione	20.218	2.55	237.17
18	Corynan-16-carboxylic acid, 16,17-didehydro-9,17-dimethoxy-, methyl ester, (16E)-	20.662	13.33	398.49
19	Anthiaergostan-5,7,9-trien-14.alpha.,15.alpha.-diol	20.851	8.21	412.6
20	Methanesulfonic acid, 17-cyano-10,13-dimethylhexadecahydrocyclopenta[a]phenanthren-17-yl ester	21.040	13.68	379.6
21	Stigmasterol	21.429	9.62	412.70
22	[1,2,4]Triazolo[1,5-a]pyrimidine-6-carboxylic acid, 4,7-dihydro-7-imino-, ethyl ester	21.518	6.11	207.19

RT = retention time, MM = molecular mass

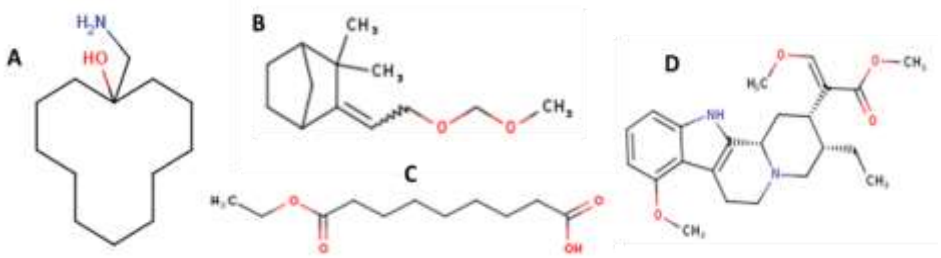

Fig.1: Drug-like compounds from *C. rostrata* fruit epicarp extract (A) Cyclododecanol, 1-aminomethyl- (B) 3-(2-Methoxymethoxyethylidene)-2,2 dimethylbicyclo[2.2.1]heptane (C) Azelaic acid, monoethyl ester (D) Corynan-16-carboxylic acid, 16,17-didehydro-9,17-dimethoxy-, methyl ester, (16E)-

Protein Targets: For azelaic acid, monoethyl ester, the top seven predicted protein targets are carbonic anhydrase I & II, vitamin D receptor, protein-tyrosine phosphatase 1B, peptidyl-glycine alpha-amidating monooxygenase, HMG-CoA reductase, and dual specificity phosphatase Cdc25A (Table 3). Inhibition of some of these proteins has been shown to have strong potential in the management of some diseases, for example, the inhibitions of carbon anhydrase II, protein-tyrosine phosphatase 1B and HMG-CoA reductase have potential in the treatment of glaucoma, diabetes and hypercholesterolemia, respectively. The top seven protein targets of cyclododecanol, 1-aminomethyl- include sphingosine kinase 1, bile acid receptor FXR, and norepinephrine transporter, which are protein targets in the treatment of cancer, cholestasis and vasovagal syncope, respectively. The top protein targets of 3-(2-Methoxymethoxyethylidene)- 2,2 dimethylbicyclo[2.2.1]heptane include dopamine

transporter, adenosine A2b receptor, and MAP kinase p38 alpha. The top seven targets predicted for Corynan-16-carboxylic acid, 16,17-didehydro-9,17-dimethoxy-, methyl ester, (16E)- include butyrylcholinesterase, delta opioid receptor and alpha-2a adrenergic receptor.

Table 3: Protein targets of drug-like constituents of *C. rostrata* epicarp

Drug-like Constituents	Protein Targets	Target Class	Prob	Disease Relevant to Target Inhibition
Azelaic acid, monoethyl ester	Carbonic anhydrase II	Lyase	0.1095	Glaucoma (Mincione *et al*., 2011)
	Carbonic anhydrase I	Lyase	0.1095	
	Vitamin D receptor	Nuclear receptor	0.0905	
	Protein-tyrosine phosphatase 1B	Phosphatase	0.0809	Diabetes, Cancer (Digenio *et al*., 2018; Kostrzwa *et al*., 2019; Rocha *et al*., 2020)
	Peptidyl-glycine alpha-amidating monooxygenase	Enzyme	0.0619	
	HMG-CoA reductase	Oxidoreductase	0.0524	Hypercholesterolemia (Simatupang *et al*., 2018)
	Dual specificity phosphatase Cdc25A	Phosphatase	0.0428	Cancer (Zhang *et al*,, 2019; Liu *et al*, 2020)
Cyclododecanol, 1-aminomethyl-	Sphingosine kinase 1	Enzyme	0.2810	Cancer (Kato *et al*., 2018; Xu *et al*., 2018)
	Bile acid receptor FXR	Nuclear receptor	0.0619	Cholestasis (Petrescu & DeMorrow, 2021)
	G-protein coupled bile acid receptor 1	Family A GPCR	0.0619	
	Alpha-L-fucosidase I	Enzyme	0.0428	
	Maltase-glucoamylase	Hydrolase	0.0428	
	Sucrase-isomaltase	Enzyme	0.0428	
	Norepinephrine transporter	Electrochemical transporter	0.0428	Vasovagal syncope (Lei *et al*., 2020)
3-(2-Methoxymethoxyethylidene)- 2,2 dimethylbicyclo[2.2.1]heptane	Dopamine transporter	Electrochemical transporter	0.0428	
	Adenosine A2b receptor	Family A GPCR	0.0428	Inflammation (Kotańska *et al*., 2021) Cancer (Sun & Huang, 2016)
	P2X purinoceptor 7	Ligand-gated ion channel	0.0428	Cancer (Lara *et al*., 2020)
	Epoxide hydrolase 1	Protease	0.0428	Neuropathic Pain (Hammock *et al*., 2021)
	Fatty acid desaturase 1	Enzyme	0.0428	
	MAP kinase p38 alpha	Kinase	0.0428	Inflammatory diseases (Machado *et al*., 2021) Viral infection (Sugasti-Salazar *et al*., 2021)
	Polyadenylate-binding protein 1	Unclassified protein	0.0428	
Corynan-16-carboxylic acid, 16,17-didehydro-9,17-dimethoxy-, methyl ester, (16E)-	Delta opioid receptor	Family A GPCR	1.0000	Chronic pain (Quirion *et al*., 2020)
	Butyrylcholinesterase	Hydrolase	0.1219	Alzheimer's disease (Tamfu *et al*., 2021)
	Serotonin 1a (5-HT1a) receptor	Family A GPCR	0.0956	CNS diseases (Mercier *et al*., 2017)
	Dopamine D2 receptor	Family A GPCR	0.0956	Psychosis (Stahl, 2017)
	Alpha-2a adrenergic receptor	Family A GPCR	0.0956	
	Adrenergic receptor alpha-2	Family A GPCR	0.0956	Erectile dysfunction (Bancroft, 2000)
	Alpha-2b adrenergic receptor	Family A GPCR	0.0956	Blood pressure (Das *et al*., 2017)

Prob: binding probability; Family A GPCR: Family A G protein-coupled receptor

The GCMS analyses of the polar and non-polar fractions of *C. rostrata* epicarp extract showed that phytochemicals with potentials that can be harnessed for human health benefits are wasted each year, as the fruit epicarp containing those phytochemicals is disposed of after the consumption of the tasty, crunchy mesocarp. Saturated fatty acids with odd numbers of carbon atoms which are present in the epicarp extract have been reported to have many health benefits, including anticancer effects and reduced risk of diabetes and heart diseases (Khaw *et al*., 2012; To *et al*., 2020). The high phytosterol content of the epicarp

extract presents potential health benefits against cancer, inflammatory diseases, obesity and free radicals (Feng *et al*., 2020; Salehi *et al*., 2021). In the structure of most protein molecules there are binding sites that affect or direct the functions of the proteins. The binding sites could be regulatory, effector or active sites to which various specific substances bind. Without considering the degree of affinity, the free energy of the ligand-protein complex or the selectivity of the ligand for the protein, the effect of the binding of a ligand to a protein molecule depends on the role of the site to which the ligand binds. The ligand-binding that results in inhibition of protein function involves binding at the regulatory or active sites, either reversibly or irreversibly; for drug development purposes, reversible ligand-binding is favoured (Rishton, 1997; Zhang *et al*., 2019b). f the compounds identified in both the polar and non-polar fractions of the epicarp extract, four compounds, two from each fraction, have the structural and functional group components that did not violate any of the five druglikeness filters used (Table 3). Azelaic acid monoethyl ester, which was identified in the non-polar fraction, is a derivative of azelaic acid; azelaic acid is known to possess antitumor, antimycotic and antibacterial properties (Breathnach, 1999; Iraji *et al*., 2007).

The *in silico* analysis identified protein tyrosine phosphatase 1B and dual specificity phosphatase Cdc25A as part of the top protein targets of azelaic acid monoethyl ester. Protein-tyrosine phosphatase 1B and dual specificity phosphatase Cdc25A have been associated with various cancers and the binding of azelaic acid monoethyl ester to these proteins could suggest its anticancer potential. The top protein targets of cyclododecanol, 1-aminomethyl- includes sphingosine kinase 1, bile acid receptor FXR and sugar metabolizing enzymes alpha-L-fucosidase I, maltase-glucoamylase and sucrase-isomaltase (Table 3). Sphingosine kinase 1 is an oncogene that is overexpressed in many cancers and its inhibition has been reported as vital in cancer therapies (Pyne *et al*., 2011; Kato *et al*., 2018; Xu *et al*., 2018). Based on structural activity relationship, cyclododecanol, 1-aminomethyl has a relatively higher probability (0.2810) of binding sphingosine kinase 1 than other protein targets (Table 4). The probability of cyclododecanol, 1-aminomethyl binding some sugar-metabolizing enzymes suggests that it might have modulatory effect in diabetes. The top protein targets of 3-(2-Methoxymethoxyethylidene)- 2,2 dimethylbicyclo[2.2.1]heptane include adenosine A2b receptor, P2X purinoceptor 7, epoxide hydrolase 1, and MAP kinase p38 alpha. Adenosine A2b receptor and P2X purinoceptor 7 are overexpressed in many cancers where each plays a non-redundant role in cancer survival and progression (Sun & Huang, 2016; Drill *et al*., 2020; Lara *et al*., 2020). The inhibition of adenosine A2b receptor and P2X purinoceptor 7 function in such cancers will therefore be vital in the management of the disease. Adenosine A2b receptor has also been reported to play a role in inflammatory diseases (Kotańska *et al*., 2021). Some other top protein targets of 3-(2-Methoxymethoxyethylidene)- 2,2 dimethylbicyclo[2.2.1]heptane such as epoxide hydrolase 1 and MAP kinase p38 alpha are implicated in inflammatory diseases and pain networks, and significant inhibitory binding of the compound to these proteins suggests potential usefulness of *C. rostrata* epicarp extract in the management of inflammatory diseases involving these proteins. The presence of Corynan-16-carboxylic acid, 16,17-didehydro-9,17-dimethoxy-, methyl ester, (16E)-, which is a yohimbine derivative, in the fruit epicarp in a relatively high proportion suggests that the epicarp extract of *C. rostrata* might elicit some sexual effects. Yohimbine is an indole alkaloid with alpha2-adrenoceptor antagonist activity, which was extracted from the dried bark of the tropical West African tree, *Pausinystalia yohimbe* (Sary & Orabi, 2012). The dried bark has been used traditionally for the management of erectile dysfunction, but there have been reports of adverse reactions from the use of yohimbine (Zanolari *et al*., 2003; Ho & Tan, 2011).

The findings show that the epicarp of *C. rostrata* is rich in bioactive compounds which could be harnessed for health benefits. Based on the constituents of the ethanol extracts of the fruit epicarp and their predicted protein targets, the crude extract or its fractions will have potential use in traditional cancer care as well as against diabetes and inflammatory diseases. The presence of a yohimbine derivate in a relatively high proportion in the polar fraction of the epicarp extract suggests that the epicarp extract could possess aphrodisiac potential. There is, however, a need to investigate the potential toxicity of the epicarp extract, as well as substantiating the predicted protein interactions and the suggestions for importance in the disease conditions mentioned.

Conclusion: Fruit wastes, particularly the epicarp, have been shown to contain useful bioactive compounds which could be useful in the treatment of several ailments and provide economic benefits after undergoing various transformative processes. *C. rostrata* epicarp contains phytochemicals which could be useful in traditional medicine and in the pharmaceutical industries.

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