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Abstract

A selected number of potential anticancer agents in phytochemicals isolated from some indigenous food and PHGLFLQDO SODQWV RI WKH :HVW $IULFDQ VXE UHJLRQ KDV EHHQ UHYLHZHG 7 NQRZOHGJH RQ WKH FKDUDFWHUL]HG DQG LGHQWL¿HG SK\WRFKHPLFDOV IURP LQ SDVW VL[RU VR GHFDGHV 6XFK FRPSRXQGV DV VDWLV¿HG WKH VWUXFWXUH DF DFWLYH DJHQWV ZHUH VHOHFWHG DQG SUR¿OHG DQG FRYHU SK\WRFKHPLFDO FO and 'miscellaneous', the latter class comprising compounds considered chemically inappropriate for the previous classes. Anticancer activities covered include: induction of carcinogen-metabolizing enzymes, selective cytotoxicity to tumor cells, reversal of multidrug resistance in cancer cells, and inhibition of metastasis. Food and medicinal uses of the source plants have also been described.

Keywords: Ant cancer; phytochem cals; West Afr ca; Alkalo ds; Flavono ds; Terpeno ds

Introduct on

Many nd genous West Afr can plants have been employed as local remed es for var ous human a lments n the trad t onal med c ne of the reg on, and as nutr t onal sources for countless generat ons [1-3]. Isolat on and character zat on of the chem cal structures for phytochem cals from useful nd genous plants have however been undertaken only for a m n mal fract on, largely because the modern techn ques of chromatography and mass spectroscopy have been explo ted by Afr can sc ent sts relat vely recently [4-6]. e s gn f cance of the latter development has been to greatly enhance an understand ng of the molecular mechan sms of act on for these solated compounds as pharmacolog cal agents. In part cular, such knowledge has been appl ed n the present d scuss on to dent fy phytochem cals from nd genous West Afr can plants w th potent al ant cancer act v t es, based on the r structure-act v ty relat onsh ps to known act ve compounds – an outcome totally unant c pated by the organ c chem sts who merely solated and character zed these phytochem cals, or whose ma n focus was on other b olog cal act v t es.

at a selected few plants would y eld the nterest ng examples d scussed here n, underscores the fact that a programmed, method cal nvest gat on of the vast ora of the reg on, n part cular, the prod g ously r ch trop cal ra n forests, would uncover a resource of un mag nable magn tude and nest mable value as ant cancer agents. A er all, t s on record, that the f rst un versally accla med and potent ant cancer agents were d scovered from plants of the Afr can cont nent and nclude such famous examples as v ncr st ne and v nblast ne, both solated from the Madagascan per w nkle plant, Catharanthus roseus G. Don (Syn V nca roseus L. nn). ese compounds were touted as:" the most successful of the plant-der ved ant tumor agents" [7]. Another s gn f cant example s maytans ne, solated from the Eth op an shrub Maytenus serrata (Celestraceae) and was one of the most prom s ng ant tumor agents d scovered by the commendable program for extens ve screen ng of ant tumor pr nc ples from plants, by the Nat onal Cancer Inst tute of the USA [8]. e Kenyan plant spec es Maytenus buchanan s reported to be a r cher source of maytans ne, y eld ng more than seven t mes the amount from M. serrata [7]. A Maytenus spec es nd genous to West Afr ca and commonly found n N ger a Ms senegalens (syn. Gymnospor a senegalens (Celestraceae). It s very l kely that a phytochem cal nvest gat on of the N ger an plant spec es may y eld maytans no ds, as s the case w th ts near relat ves n East Afr ca.

e prof led phytoch em cals are grouped as potent al "Cancer Chemoprevent ve" and "Cancer Chemotherapeut c" agents and cover many of the known phytochem cal classes such as alkalo ds, avono ds, terpeno ds and 'm scellaneous', the latter class compr s ng compounds cons dered chem cally nappropr ate for the prev ous classes. Ant cancer act v t es covered nclude: nduct on of carc nogen-metabol z ng enzymes, select ve cytotox c ty to tumor cell l nes, reversal of mult drug res stance n cancer cells, and nh b t on of metastas s, w th a few spec f c examples selected to llustrate the po n n some nstances, ant cancer potent als of the phytochem cals have been d scerned from relevant exper mental data. A s gn f cant example n th s regard would be the case of the b avono d, kolav ron wh ch had h therto been known as a potent hepatoprotect ve agent [9,10] and wh ch, n the author's research exper ence, gave nd cat ons of a potent al human cancer chemoprevent ve agent aga nst a atox n B1-nduced hepatocarc nogenes s [11]. e d etary appl cat ons as well as trad t onal med c nal uses of the source plants, as pract ced n the spec f c local env ronments of or g n, have also been descr bed. Such dent f ed compounds however, ls t wa t relevant b olog cal act v ty tests, before conf rmat on of suggested ant cancer potent als.

Cancer Chemoprevent ve Agents

A. Induct on of carc nogen metabol z ng enzymes

From fresh seeds of an nd genous plant, B tter Kola Garc n a

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kola Heckel (Gutt fe ae), was s olated kolav ron (KV), a m xture of three b avono ds; GB-11 (1), GB-2 (2) and kola avanone, KF3 (3), [12]. Prev ous stud es had demonstrated that kolav ron reduced hepatotox c ty n exper mental an mals [12-14]. A subsequent study by th s author, nd cated that t could nh b t a atox n B1 (AFB1)- nduced genotox c ty n the human l ver-der ved HepG2 cells [11]. Kolav ron, at the h ghest tested concentrat on of 90 µM reduced AFB1- nduced unscheduled DNA synthes s, measured as H-thym d ne ncorporat on nto HepG2 cells, by 53%. e latter study further demonstrated that kolav ron's mechan sm of act on nvolved an nduct on of the AFB1-detox cat ng enzymes such as cytochrome P450 3A4, and glutath one S-transferases A1-1, A2-2, M1-B, nd cated by a three-fold ncrease n the transcr pts for the enzymes, and a two-fold ncrease for GST A1-1 and A2-2 prote n. Kolav ron therefore appeared to have a chemoprevent ve potent al n nh b t on of human AFB1- nduced genotox c ty and poss bly, carc nogenes s (F gures 1 and 2).

B tter kola (C. carc n a kola) seed from wh ch kolav ron was obta ned, s an ed ble nut frequently consumed as "kola", or guest snack both at homes and at soc al gather ngs n the southern parts of N ger a. Two b avono ds structurally s m lar to kolav ron were also s olated from the stem bark of G. dens ven a [15] and named, morello avone (4), and ts methyl ether der vat ve, O-methylfukugetin (5) [15]. Many other b avono ds have been s olated from G. carc n aspec es of the Douala-Edea Forest Reserve of West Cameroun, some of wh ch could d splay cancer chemoprevent ve act v ty s m lar to kolav ron [16]. ese compounds are yet to be nvest gated for poss ble ant cancer act v ty.

In a follow-up study, the potent als of kolav ron as a ple otrop c nducer of hepatoprotect ve genes, espec ally n a atox n B1 tox cat on of human hepatocytes, was evaluated by gene m croarray assay [17]. s work employed human pr mary hepatocytes (HPH) separately treated w th AFB1 (2.0 µM /L) and KV (90 µM /L) then a comb ned pretreatment w th kolav ron before AFB1, wh le gene express on analys s employed the A ymetr x Gene 1.0ST array conta n ng the ent re human genome. Results suggested a central role for the human "Inh b tor of DNA b nd ng 1, ID1 gene" (Gene ID: 3397; MIM: 600349), wh ch was s gn f cantly up-regulated to about three-fold message levels, n all three treatments, as well as a few other genes that were separately regulated [17].

Figure 1: 1/2/3
1: GB1 (Rl = R2 = R3 = R5 = H, R4 = OH)
2: GB2 (Rl = R2 = R4 = R5 = H, R3 = OH)
3: KF (R3 = R5 = H, Rl = R4 = OH, R2 = OCH3)

Figure 2: 4/5
4: R = OH
5: R = OCH3

Cancer Chemotherapeut c Agents

A. Cytotox c ty to tumor cells

) Alkalo ds: ***Benzophenanthrid ne alkalo ds:*** e benzophenanthr d ne alkalo ds, n t d ne chlor de (6), (and a new der vat ve, 6-methoxy-5,6-d hydron t d ne, were s olated from Fagara macrophylla [18]. Both compounds were shown to be about equ potent n the P-388 mouse leukem a system, g v ng h gh T/C values of 240 and 260% respect vely, at doses of 30-50 mg/kg. Another der vat ve Fagaron ne, (7), was s olated from the Ghana an and N ger an plant, Fagara zanthoxyloides Lam. (Rutaceae) [19]. Fagaron ne (7) l ke ts relat ve, n t d ne, s act ve n both the P-388 and L-1210 leukem a test systems [20]. A latter study suggests that the structural determ nants for ant tumor act v t es n benzophenanthr d nes, nclude the ex stence of a planar, cat on c resonance hybr d between the keto-am ne and ZW tter on c forms n neutral med a, and a phenol c OH at C-7 [21]. It therefore becomes necessary to rev ew the act v t es of the subsequent d scovered der vat ves as descr bed below (F gures 3 and 4).

One such alkalo d bear ng structural s m lar t es to a known ant tumor compound s palmat ne (8) (extracted among other alkalo ds, from roots of the West Afr can cl mb ng shrub, Rh g ocarya racem fera [22]. Palmat ne (8), s structurally s m lar to coralyne sulfoacetate (9), (the latter be ng one of the related alkalo ds of n t d ne chlor de, wh ch showed ant leukem c act v ty [23].

A decoct on of the stem bark of Fagara macrophylla s taken as an ant sept c for the gen tour nary tract, and s also appl ed as a rubefac ent n toothaches, n the folk med c ne of N ger a [16]. Extracts of the roots are also used for coughs and colds. Fagara racem fera Hems (Men spermaceae), s a cl mb ng shrub nd genous to the forests of Ghana and other parts of West Afr ca, whose roots are added to palm w ne, and extracts of the plant used med c nally as nasal drops, and as an aphrod s ac (F gure 5) [22].

Pept de alkalo ds: For pept de alkalo ds, the s olat on of 2 new cycl c octapept des des gnated phakell stan 10 (10) and phakell stan 11 from the mar ne sponge Phakell a sp. has been reported [24]. Both compounds demonstrated s gn f cant cytotox c act v ty aga nst the P-388 leukem a cell l ne, hav ng ED50 values of 2.1 and 0.2 µg/mL, respect vely. A structurally related cycl c octapept de named cyclogoss n B (11), was subsequently s olated from latex of the plant

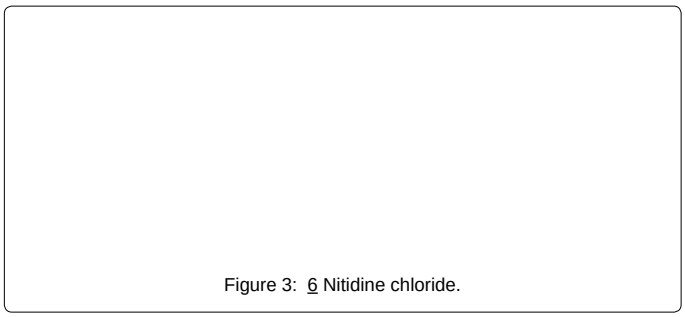

Figure 3: 6 Nitidine chloride.

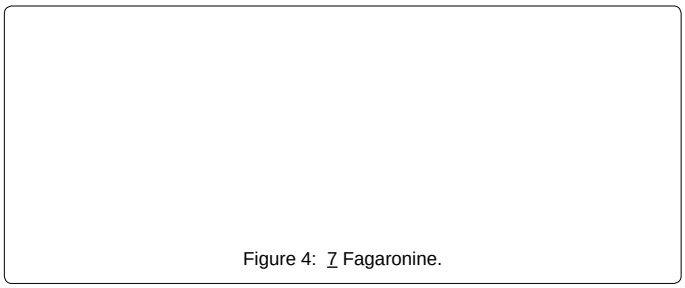

Figure 4: 7 Fagaronine.

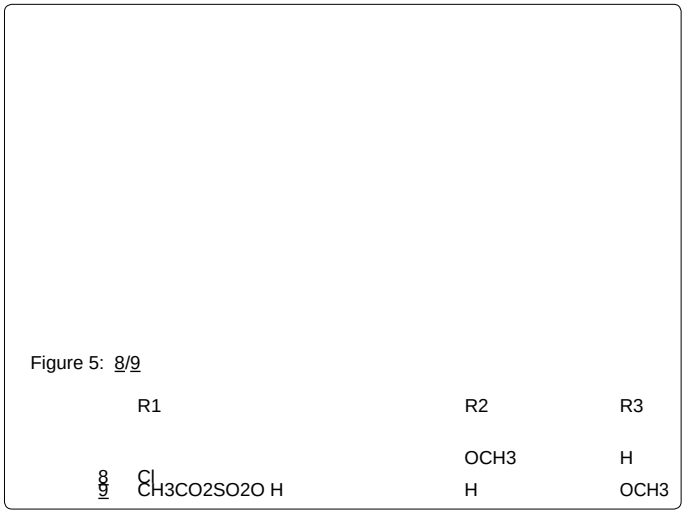

Figure 5: 8/9

	R1	R2	R3
8	Cl	OCH3	H
9	CH3CO2SO2O H	H	OCH3

Jatropha gossypifolia (Euphorbiaceae) [25]. Cyclogossin B is yet to be investigated for possible cytotoxic activity. Structure-activity relationships of cytotoxic cyclic octapeptides have not been determined but on the basis of the close structural similarity between phakellistan 10 (10) and cyclogossin B (11), it is reasonable to expect that the latter may also display some cytotoxic activity.

The fresh latex of Jatropha gossypifolia is reportedly applied to infected wounds and ulcers and a decoction of the plant is used to treat fever in Togo and Senegal, where the plant bears the vernacular name of “lumulum” (Figures 6 and 7) [25].

Other cyclopeptide alkaloids have been isolated from local plants, including a number of such compounds from the root bark of Hymenocardia acida beginning with the first such isolate named hymenocardine [26]. Subsequently, hymenocardine was re-isolated along with its derivatives including one with a hydroxyl- in place of a carbonyl group that was named hymenocardol, a hymenocardine N-oxide, and a new cyclopeptide alkaloid containing an unusual histidine moiety named hymenocardine-H [27]. In a previous work, it had been reported that the methanol extract from the same part of the plant exhibited cytotoxic activity against a panel of human tumor cell lines [28].

Hymenocardia acida Tul. (Phyllanthaceae) is a shrub or small tree indigenous to the African Savannah where the leaves and roots of the plant are used to treat malaria in traditional African medicine [29]. roots of the plant are also said to be used as antimalarial in Nigeria [30].

) Terpenoids: Of the numerous reports of tumor cytotoxic terpenoids, one example selected from indigenous West African plants would serve to illustrate the potency of anticancer activity that may be found in this group.

a) *Sesquiterpenoids*: ecytotoxic and antitumor sesquiterpenes have been found almost exclusively among the germacrane, guaiane eudesmane and elemane sub-groups. Almost without exception, a common structural factor for these active compounds appears to be the possession of an -methylene- -lactone ring. e latter chemical grouping, alone, or in addition to other reactive groups such as -enones, , -unsaturated lactones, ketones, and esters or epoxides, have been hypothesized to be subject to nucleophilic attack, resulting in the

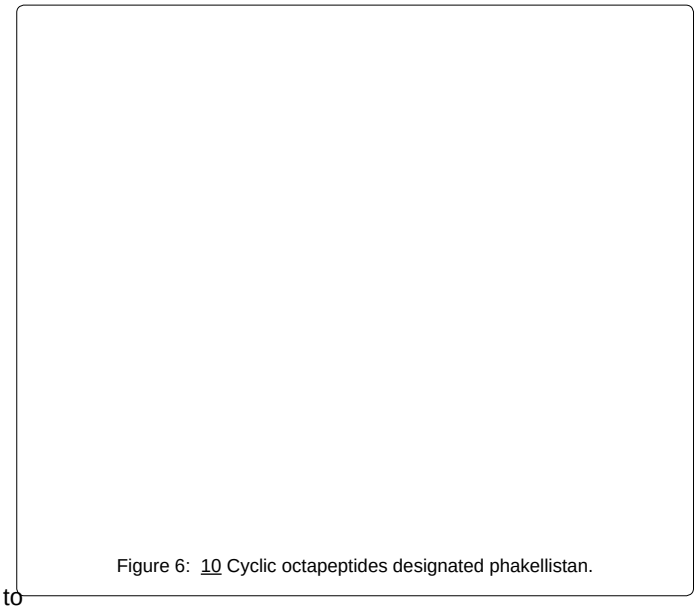

Figure 6: 10 Cyclic octapeptides designated phakellistan.

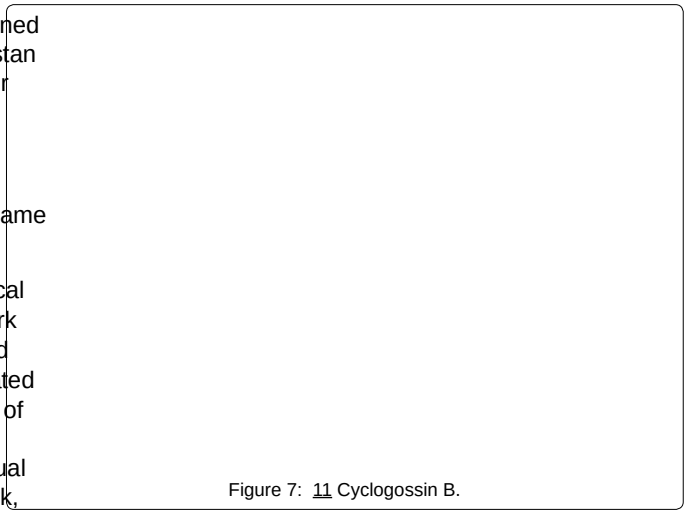

Figure 7: 11 Cyclogossin B.

alkylat on of b olog cally s gn f cant macromolecules, and consequently lead ng to cancer cell death [31].

A typ cal example s the act ve compound vernodal (12), from the elemanol de sub-group solated from the dr ed leaves of Vernon a amygdal na Del. [32] and hav ng s gn f cant n v tro cytotox c act v ty aga nst the Walker carc noma 256 w th an ED50 of 1.8 µg/mL [32]. 12 was re-solated from Vernon a amygdal na along w th two other elemanol de lactones, vernodalol and a new compound d hydrovernodal (13) [33]. e poss ble ant cancer act v t es of the latter two compounds have not yet been nvest gated (F gure 8).

A new ant cancer sesqu terpene lactone has been solated from Vernon a amygdal na and named:

“vernodal nol” [34]. e compound wh ch possesses the requ s te -methylene- -lactone rng postulated as the structural requ rement for ant cancer act v ty n the sesqu terpene lactones, d splayed modest cell growth nh b tory act v ty (nh b t on of DNA synthes s) n the human mammary adenocarc noma cell l ne MCF-7, where values of 34% and 40% (P <0.025) growth nh b t on were obta ned at concentrat ons of 25 and 50 g/mL, respect vely [34].

Vernon a amygdal na (b tter leaf) s a h ghly valued food tem as the leaves are a popular vegetable for soups among the Igbo of southern N ger a. Med c nal appl cat ons of amygdal na nclude use of the tw gs as “chew ng st ck”, or local toothbrush, wh ch are chewed as a stomach c ton c and appet zer. A decoct on of the leaves s taken as an ant pyret c and laxat ve, and for coughs [16].

v) M scellaneous: s category covers phytochem cals possess ng s gn f cant n v tro cytotox c t es aga nst tumor cell l nes, and wh ch, for reasons of proper nomenclature, may not be ncluded n the other class cal groups. For reasons of space and brev ty, only one example is d scussed here.

Gamma-l nolen c ac d: Pat ents w th mal gnant pr mary gl omas or mammary adenocarc nomas have a poor prognos s as common therapeut c approaches are relat vely ne ect ve. Interest ngly, an ed ble, essent al polyunsaturated fatty ac d (PUFA), -l nolen c ac d (GLA, 14) was found to be select vely cytotox c to gl omas and other tumor types [35,36], wh le normal cells are largely una ected. Although the mechan sm for th s select ve cytotox c ty s poorly understood, free rad cal generat on w th l p d perox dat on from PUFA supplementat on s generally bel eved to play a role [35,36]. However, the latter assumpt on s awed on many counts, not least of wh ch s the fact that h gher members of the PUFAs, conta n ng h gher unsaturat on and presumably better able to generate the assumed tox c free rad cals are ne ect ve (F gure 9).

s author proposed a plaus ble mechan sm for GLA- nduced cytotox c ty to tumor cells, part cularly gl omas and mammary

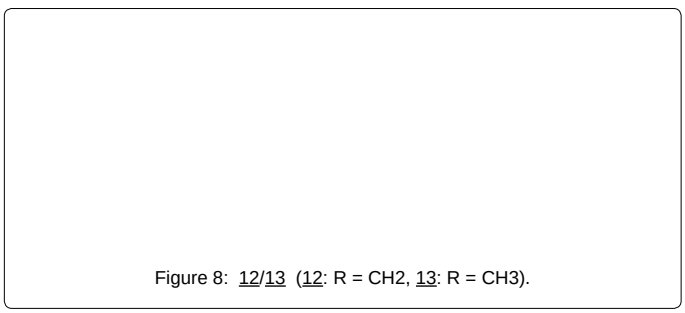

Figure 8: 12/13 (12: R = CH2, 13: R = CH3).

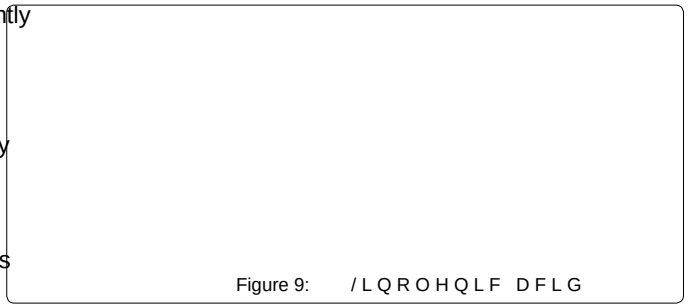

Figure 9: / L Q R O H Q L F D F L G

adenocarc nomas [37]. e art cle was publ shed n 2001 and t tled: “Repress on of cellular anapleros s as the hypothes zed mechan sm of GLA- nduced tox c ty to tumor cells” [37]. About four years later, workers n another laboratory [38] ndependently prov ded corroboratory exper mental support for th s hypothes s, thus strengthen ng the theory and conferr ng sc ent f c leg t macy on the postulate. ere s hope that th s postulate would serve as a bas s for the des gn of new therapeut c agents aga nst the dreaded gl omas an metastat c mammary carc nomas.

GLA, the tumor cell cytotox c agent, was subsequently shown to be present n large amounts, as ts b ochem cal precursor, l nole c ac d, n the commonly eaten (South-Eastern N ger a) o l bean seed (‘ugba’ or ‘upkaka’: Pentaclethra macrophylla) n a related art cle co-publ shed by th s author [39].

In a related ant cancer act v ty of a d etary l nolen c ac d obta nable from nd genous plants, d etary supplementat on w th 0.01% and 0.1% o l from b tter melon (Momord ca charant a) wh ch s r ch n c s(c)9, trans(t)11, t13-conjugated l nolen c ac d (CLN), s gn f cantly reduced the s nc dence of azoxymethane (AOM)- nduced colon c aberrant crypt foc (ACF) n male 344 rats [40]. e authors suggested that the mechan sm of CLN suppress on of AOM- nduced colon carc nogenes s m ght, n part be through mod f cat on of l p d compos t on n the colon and l ver and/or ncreased express on of PPARgamma prote n level n the colon mucosa.

Momord ca charant a (Cucurb taceae) s a plant of common use n the trad t onal med c ne of West Afr ca as an ant malar al [41], n the treatment of measles [42] n N ger a, and for the treatment of gastro ntest nal and v ral sease n Togo [43].

B. Reversal of mult -drug res stance (MDR)

An llustrat ve example w ll be c ted here, from the alkalo d class of phytochem cals.

e b sbenzyl soqu nol ne alkalo ds: F gure 10 Two known b sbenzyl soqu nol ne alkalo ds, sotr lob ne (15), and tr lob ne (16), were solated from an extract of the v ne, Stephan a japon ca [44]. Us ng the b c nchon n c ac d assay, both compounds were shown to be act ve n revers ng doxorub c n res stance n the adr amyc n-res stant human breast adenocarc noma cell l ne, MCF-7/ADR, w th sotr lob ne (15) be ng more act ve than tr lob ne (16) and equ potent w th the reference compound verapam l [44]). S nce the only structural d erence between (15) and (16) s the methyl group at N-2', the greater e cacy of 15 suggests that a tert ary am ne s preferred at th s pos t on to a secondary am ne. e authors also suggested that the ncreased l poph l c ty nduced by presence of an extra methyl group in 15 may contr bute to the enhanced act v ty, s nce MDR nh b tors are known to be l poph l c.

Figure 10: 15 – 18
15: R1 = R2 = CH3; 16: R1 = H, R2 = CH3; 17: R1 = CH3, R2 = H;
18: R1 = R2 = CH3, B = Aromatic.

Other b sbenzyl soqu nol ne alkalo ds, cocsul ne 17) and tr g llet m ne (18), have been reported from extracts of the whole plant of Tr cl s a d ctyophylla D els. (Men spermaceae), [45], and from leaves of T. g llett (DeW ld.) Staner, were solated four more such compounds named obameg ne, steb s m ne, g llet ne and sog llet ne-N-ox de, the last two descr bed as new b sbenzyl soqu nol ne d benzo-p-d ox n alkalo ds [46]. e remarkable structural s m lar ty between these Tr cl s a solates and the MDR-act ve compounds sotr lob ne (15) and tr lob ne (16) ra ses the hope that some may be found act ve, f tested. Of part cular nterest n th s regard s cocsul ne (17), wh ch s almost dent cal w th the h ghly act ve sotr lob ne (15) and d er ng only n the possess on of a hydroxyl, rather than a methoxy subst tuent at pos t on 12. S m larly, tr g llet m ne (18) may d splay a h gher act v ty than tr lob ne (16) s nce the only structural d erence between the two s that the “B” r ng n the former s aromat c wh ch should stand t n good stead. For nstance, possess on of a term nal aromat c group, as well as an nternal -env ronment are two of the structural requ rements for reversal of MDR-act v ty n these compounds [44].

A b sbenzyl soqu nol ne alkalo d named ‘cyclean ne’ has been solated from ethanol extract of

Tr cl s a subcordata and shown to potently (IC50<2 µg/mL) nh b t tumor cell growth n the ovar an cancer, Ovcar-8 and A2780 cell l nes, us ng the Sulforhodam ne B assay [47]. e IC50 of cyclean ne on human normal ovar an surface ep thel al cells was 135, thus suggest ng modest select v ty toward cancer cells. Mechan sm of act on for cyclean ne was further nd cated to be through apoptos s as shown by act vat on of caspases 3/7 and cleavage of poly(ADP-r bose) polymerase [47].

From leaves of another nd genous West Afr can plant, Tr cha cora fun fera, was solated a new m no b sbenzyl soqu nol ne alkalo d named, ‘t l afun m ne’ [48]. e authors also descr bed two other b sbenzyl soqu nol ne alkalo ds solated from the same source as, sotetrandr ne and thalrugos ne. ese compounds are yet to be nvest gated for poss ble mult drug res stance act v ty. Tr cyl s a subcordata Ol v (Men spermeaceae) was descr bed by the authors as a med c nal plant trad t onally used for the treatment of var ous d seases n West Afr ca [47], wh le Tr l acora fun fera (Men spermaceae) s a woody cl mber of Ghana and West Afr ca that has been used as a med c nal n the treatment of numerous a lments [48].

C. Inh b t on of metastas s

A s gn f cant example n th s category would be the report of work nvolv ng the phytochem cal, (+)-catech n (19). s compound has been, almost exclus vely, the only avan nvest gated for ts e ects n cancer. Prom nent among the ant cancer e ects reported are ts ant ox dant e ect n nh b t ng the auto-ox dat on of l nole c, and methyll nole c ac ds [49], and the n v tro nh b t on of metastas s as descr bed below. In the latter study, the ant -metastat c potent al of some phytochem cals, nclud ng (+)-catech n, aga nst the h ghly nvas ve, Dunn ng rat prostate adenocarc noma cells (R3327-5´A), was nvest gated [50]. Among the nvas ve parameters stud ed, were matr gel membrane nvas on by the trans-well assay; gel zymography assay and Northern analys s, for the matr x metalloprote nases (MMP-2 and MMP-9)’s act v ty and gene transcr pt on respect vely; as well as Western mmunoblot assay, for gene express on analys s of the membrane-assoc ated prote ns -, - and -caten ns. Results nd cated that catech n at 25 µM, s gn f cantly decreased matr gel membrane nvas on of the prostate tumor cells by 24% and also nh b ted -caten n prote n levels by 58% (P<0.01), (F gure 11) [50].

A s gn f cant N ger an food source from wh ch (+)-catech n (19), (and ts der vat ves have been solated s descr bed below was obta ned from f ve ed ble spec es D oscorea (yams), nd genous to N ger a [51]. e f ve yam spec es, and the r cult vars or N ger an (Igbo) names were g ven as D oscorea alata a, two cult vars (Om nelu and UM 680); D. bulb fera L, (Adu); D. cayanens s Lam. (Oku); D. dumetorum Pax. (Ona); and D. rotundata Po r., f ve cult vars (Ab , Ekpe, Nwopoke, Ob aturugo and Okwocha), [51]. Yams are a starchy staple and h ghly pr zed foodstu n N ger a and ne ghbor ng countr es. O en, the wealth of a farmer n the Igbo-speak ng areas of N ger a s determ ned by the quant ty of yams stocked.

In an analys s for secondary plant metabol tes contents of kola nuts (Cola n t da) popularly consumed n N ger a and other West Afr can countr es, (+)-catech n was shown to be present n the h ghest amount among the phytochem cals found [52]. ree var et es of kola nuts (Colan t da alba, Cola n t da rubra A. Chev, and Cola acum nata Schott & Endl) were analyzed and the phytochem cal contents g ven n decreas ng order of quant ty as: (+)-catech n (27-37 g/kg), ca e ne (18-24 g/kg), (-)-ep catech n (20-21 g/kg), procyan d n B 1 [ep catech n-(4beta-->8)-catech n] (15-19 g/kg), and procyan d n B2 [ep catech n-(4beta-->8)-ep catech n] (7-10 g/kg) [52,53]. Kola nuts would therefore const tute a s gn f cant source of the ant cancer compound (+)-catech n, espec ally for people n the northern parts of N ger a where kola nut consumpt on s a very popular past me.

Figure 11: 19 (R = Galloyl-)

Conclus on

e object ve of th s rev ew has been to pr mar ly h ghl ght the ex stence of prom s ng ant cancer potent als nherent n phytochem cals from nd genous West Afr can plants of common usage, as local food or n the trad t onal med c ne of the area. Ethnopharmacolog sts and other sc ent sts n related f elds on the Afr can cont nent are hereby exhorted to spear-head more of such stud es a med at espous ng the mmense benef ts accruable from a rev val of nterest n th s relat vely neglected pool of valuable resource.

It s however mportant to stress that e orts should be made to solate and character ze the spec f c act ve pr nc ples respons ble for ant cancer act v ty. e common pract ce of ascr b ng act v t es to crude extracts, wh le understandably attr butable to a pauc ty of research fac l t es, would hamper a des rable apprec at on of mechan st c ns ghts and deter necessary contr but on to the nternat onal knowledge base on th s subject. s d scuss on n wh ch the chem cal structures of act ve agents are presented and evaluated, llustrates the advantages to be ga ned n the prescr bed approach.

F nally, the author once more w shes to draw attent on to the mm nent threat posed by rap d deforestat on of trop cal forests, and the loom ng danger that rare curat ve plants would be lost forever, f mmed ate prevent ve act on s not taken.

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