Journal of Medicinal and Chemical Sciences 5 (2022) 518-536

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Review Article

Influence of Albocarbon-cyclic Hybridization on Biomedical Activities: A review

Yasser Fakri Mustafa*, Moath Kahtan Bashir, Mahmood Khudhayer Oglah

Department of Pharmaceutical Chemistry, College of Pharmacy, University of Mosul, Ninavah-41002, Iraq

ARTICLE INFO

Article history

Received: 2022-01-03
Received in revised: 2022-01-16
Accepted: 2022-01-20
Manuscript ID: JMCS-2201-1382
Checked for Plagiarism: **Yes**
Language Editor:
Ermia Aghaie
Editor who approved publication:
Dr. Zeinab Arzehgar

DOI:10.26655/JMCHEMSCI.2022.4.8

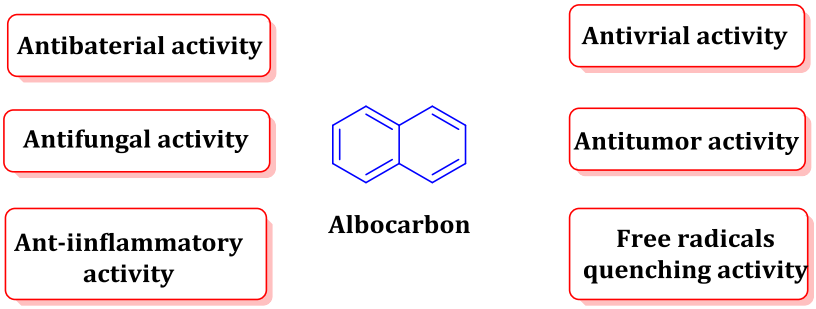
KEYWORDS

Albocarbon
Hybridization
Cyclic moieties
Pharmacological activities

ABSTRACT

There is an excellent demand in biomedical sciences for novel drug-like compounds with the best therapeutic benefits and minor adverse effects. The albocarbon moiety is seen to be abundantly available in nature, prompting various investigations to isolate albocarbons and investigate their pharmacological activities. Synthetic albocarbons show various biological properties, including antioxidant, antibacterial, antiproliferative, anti-inflammatory, antifungal, and antiviral effects. The consequences of hybridizing cyclic molecules with albocarbons on their bioactivities have been studied widely in the literature. The bulk of these studies revealed that this hybridization might improve the pharmacological properties of the mother albocarbons. This comprehensive review, which described the most critical and recent examples of such studies, emphasized the structural features of the produced hybrids as potentially bioactive frameworks.

GRAPHICAL ABSTRACT



* Corresponding author: Yasser Fakri Mustafa
✉ E-mail: Email: Dr.yassermustafa@uomosul.edu.iq

Introduction

General View

Albocarbon, as illustrated in Figure 1, is almost like an arene consisting of two aromatic rings welded together in the ortho locations. It manifests as a crystalline powder with a distinct mothball aroma [1].

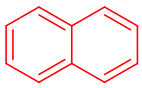


Figure 1: Albocarbon's chemical structure

Different biological actions have been discovered in the natural, semisynthetic, and synthetic medications that include albocarbon or one of its derivatives in their chemical compositions [2]. Nafacillin, naftifine, tolnaftate, and terbinafine are examples of these medications, as illustrated in Figure 2. The first albocarbon is considered an antibacterial medication, while the second and third are antifungal drugs [3].

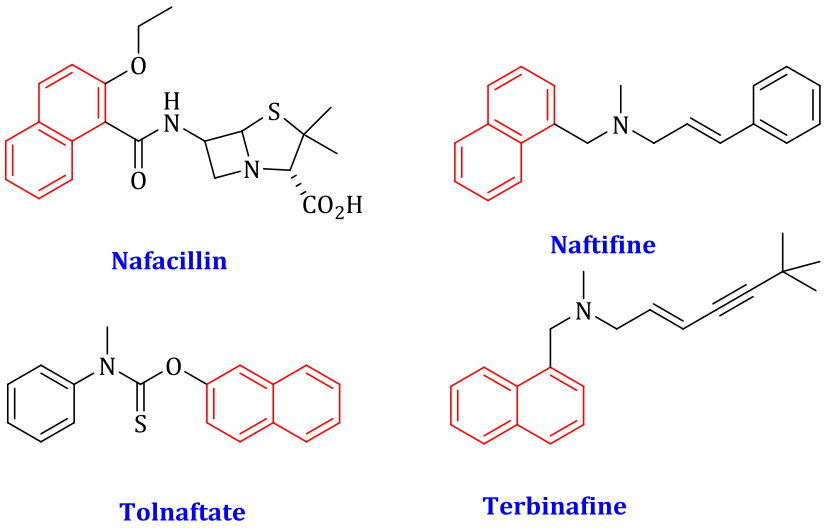


Figure 2: Chemical structures of presently available albocarbon-based medicines

Antibacterial Activity

The utilization of antibacterial agents is on the rise, increasing antibiotic-resistant bacteria [4,5]. This phenomenon necessitates further research and innovation of potential antibacterial medications capable of battling these resistant strains [6]. In this concern, many researchers have looked at the antibacterial effect of grafting various cyclic moieties with albocarbon-containing compounds [7-15].

Many functionalized indoles were synthesized by Ashraf et al. and grafted to the albocarbon nucleus. *In vitro* testing was done on the antibacterial effectiveness of the hybrids (Figure 3) against Staphylococcus aureus (S. aureus) and methicillin-resistant Staphylococcus aureus (MRSA). According to the findings of this study [7], the hybrids with the best antibacterial property had 5-hydroxy-, 5-cyano-, or 5-chloro-indole in their frameworks.

Chopra *et al*. [8] created a novel naphthylamine analogs with a substituted azetidin-2-one ring. The antibacterial activity of the obtained albocarbon-based compounds was tested using S. aureus, E. coli, P. aerogenosa, and B. subtilis. Some of the hybrids investigated, designated 4a, 4e, 4g, and 4f (Figure 4), had intriguing antibacterial property, with inhibition zones extending from 9 to 19 mm. Ampicillin, the conventional antibacterial medication utilized in this study, inhibited the test microorganisms with inhibition zones extending from 15 to 45 mm.

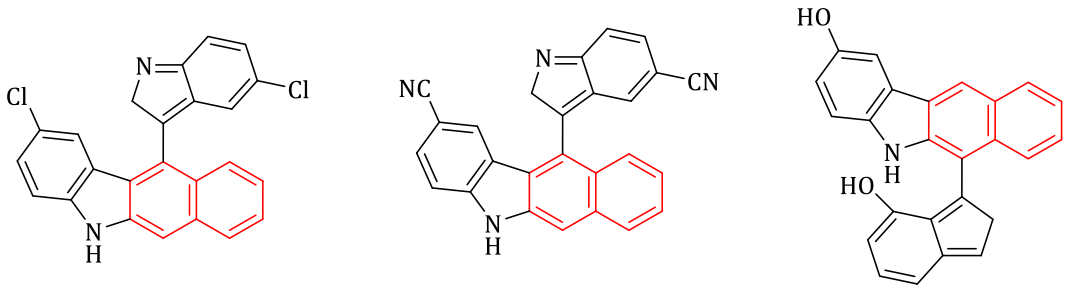
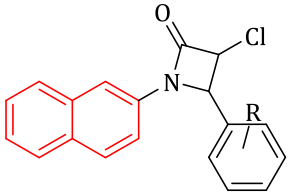


Figure 3: Chemical structures of the albocarbon-derived hybrids as illustrated by Ashraf *et al.*



R:
4a = 4-OHC_6H_4
4e = C_6H_5
4g = $4ClC_6H_4$
4f = $3NO_2C_6H_4$

Figure 4: Albocarbons having potent antibacterial activity produced by Chopra *et al*.

A new series of hydrazines hybridized with the albocarbon have been synthesized by Sivasankari and Mary. The antibacterial activity of these hybrids was tested versus a variety of Gram-negative (E. coli, and P. aerogenosa) and Gram-positive (B. subtilis, S. pyogenes, and S. aureus) bacteria using an agar-disc diffusion approach. Hybrids 3, 5, and 6 (Figure 5) were active versus the two test bacterial forms. Also, the antibacterial activity was greatest versus S. aureus and E. coli bacterial strains [9].

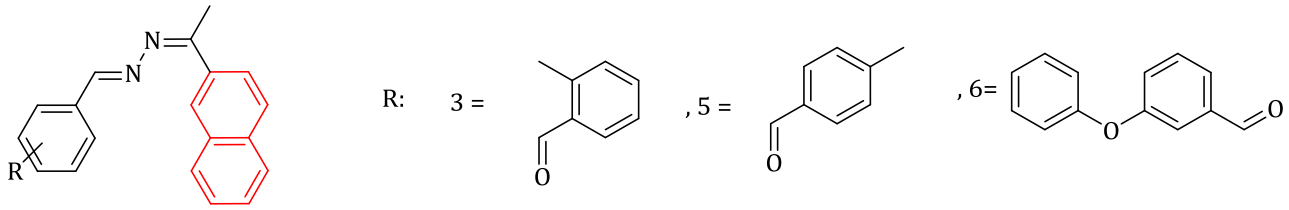


Figure 5: Albocarbons with a wide-ranged spectral antibacterial activity created by Sivasankari and Mary

Kumar *et al*. [10] developed a series of albocarbon-piperazine hybrids evaluated for antibacterial activity against some Gram-negative and Gram-positive strains bacteria, including B. subtilis, S. aureus, and E. coli, and K pneumonia, using a cup-plate diffusion methodology. The hybrids numbered 4b, 4c, and 4e (Figure 6) were shown to have the most powerful action against the microorganisms tested, with inhibition zones spanning from 2 to 6 mm. Ciprofloxacin was the standard antibacterial medication utilized in this investigation, with inhibition zones ranging from 10 to 14 mm.

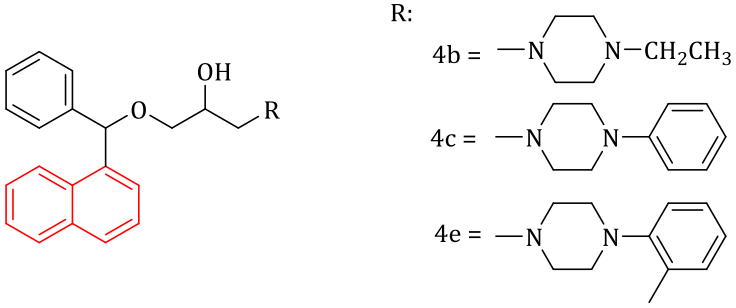
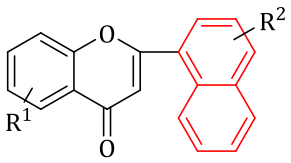


Figure 6: Albocarbons produced by Kumar *et al*. having potent antibacterial action

Many albocarbon-flavone hybrids have been synthesized by Zangade *et al.* and tested as potential antibacterial candidates. This *in vitro* investigation was employed tetracycline as a gold standard and disc-diffusion technique to test the antibacterial efficacy of these hybrids versus E. coli and S. aureus. The findings indicated that in terms of antibacterial activity, the chloride-substituted hybrids IIc and IIf (Figure 7) outperformed the reference antibiotics [11].

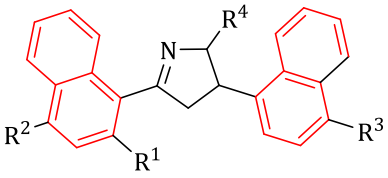


IIc
R^1= 6,8-Cl
R^2= 4-Br

IIf
R^1= 8-I, 6-Cl
R^2= 2-OCH_3

Figure 7: Albocarbons produced by Zangade *et al*. having potent antibacterial efficacy

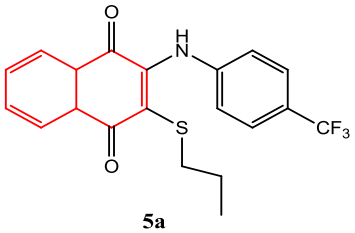
A new set of albocarbon-pyrazoline hybrids have been developed and tested as antibacterial applicants by Azarifar and Shaebanzadeh. The employed strains were P. mirabilis, E. coli, K. pneumonia, S. aureus, S. typhi, and S. dysentery. This research was carried out using a well-known approach, and the MIC values obtained were compared to those of chloramphenicol, which was used as a control. Compared to the others, the 3cg, 3eh, 3ci, 3di, and 3ei (Figure 8) hybrids with chloro, hydroxy, and dimethylamino substituents the albocarbon rings were shown to be the most efficient [12].



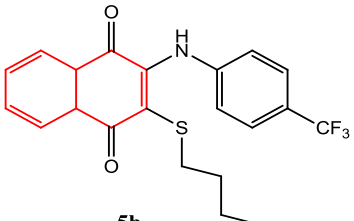
3cg
R_1= OH, R_2= H, R_3= NMe_2, R_4= H
3eh
R_1= OH, R_2= Me, R_3= NMe_2, R_4= ph
3ci
R_1= OH, R_2= H, R_3= NMe_2, R_4= $CONH_2$
3di
R_1= OH, R_2= Cl, R_3= NMe_2, R_4= $CONH_2$
3ei
R_1= OH, R_2= Me, R_3= NMe_2, R_4= $CONH_2$

Figure 8: Albocarbons created by Azarifar and his colleagues

Kara *et al*. [13] produced several phenylamino-thionaphthaquinone hybrids. They tested them against various pathogenic bacterial strains, including P. mirabilis, E. coli, E. faecalis, S. aureus, P. aerogenosa, S. epidermidis, and K. pneumonia. The hybrids **5a** and **5b** (Figure 9) were the most effective against S. aureus, with MIC values of 1.22 and 19.53 g/mL, respectively, compared to the cefuroxime MIC value of 1.2 g/mL. These findings suggested that greater study into these hybrids' effectiveness as antibacterial medications should be conducted.



5a



5b

Figure 9: Chemical structures of the hybrids produced by Kara *et al.* having potent antibacterial action

Shakh *et al*. [14] synthesized a series of 1,4-naphthoquinone grafted to the diverse 1,2,4-triazole-3-thiones in a work comparable to the previous one. Antibacterial ability of these hybrids was evaluated versus E. coli and S. aureus using the agar-diffusion technique with

Vancomycin as a reference drug. Compared to the vancomycin's inhibition zone of 11.3 mm, the hybrids numbered 5 and 7 (Figure 10) were shown to be particularly effective against S. aurous, with inhibition zones of 10.4 and 10.7 mm, respectively.

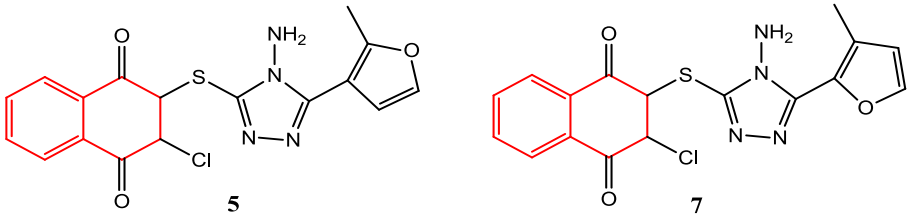


Figure 10: 1,4-Naphthoquinone hybrids produced by Shakh *et al.* having potent antibacterial activity

The antibacterial efficacy of novel congeners produced by grafting albocarbon moiety with coumarins was examined against many Gram-negative and -positive pathogenic bacterial strains, including E. coli, S. aurous, B. subtilis, and P. vulgaris. Compared to the standard antibiotics streptomycin, the hybrids **2b** and **2e** (Figure 11) were the most effective. The replacement of a methoxy group at the 8th position of coumarin has a considerable favorable influence on the antibacterial activity of these congeners, according to the authors of this work [15].

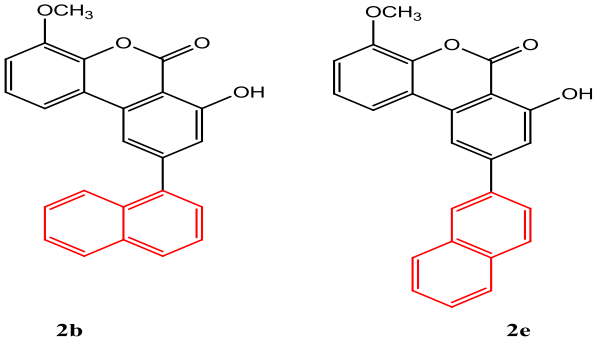


Figure 11: Albocarbons having potent antibacterial action

Antifungal Activity

Chopra *et al*. [8] developed some albocarbon-thiazolidinone hybrids. They assessed their antifungal activity against Candida albicans (C. albicans) utilizing an agar-plate diffusion strategy with amphotericin B as a baseline. With inhibition zones of 9 mm and 13 mm, respectively, the hybrids 5b and 5e (Figure 12) were considerably more effective than the reference. These findings suggested that by grafting the N-heterocyclic moiety with albocarbon, a promising framework for developing antifungal medicines may be created.

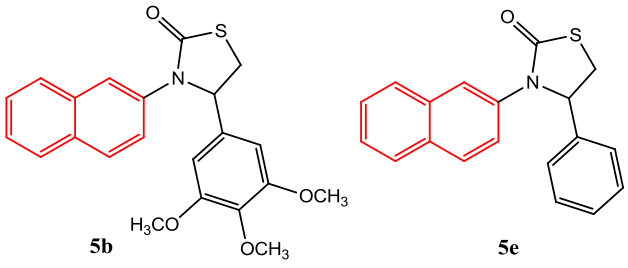


Figure 12: Albocarbons produced by Chopra and his colleagues with potent anti-candida action

Ghiya and Joshi used a one-pot green synthesis approach to create a new class of albocarbon hybrids. Underneath the influence of microwave heating, various substituted aryl carbonyl compounds were fused with albocarbon-1-sulfonhydrazide. Using a potato-dextrose agar as the nutrition medium and fluconazole as the reference, these hybrids were evaluated against Aspergillus niger (A. niger) and Candida albicans, respectively. According to the findings, the

created hybrids, notably the 3h and 3i (Figure 13), demonstrated high to excellent antifungal activity. The inhibition zones for hybrid **3h** against A. niger and C. albicans were 10 mm and 12 mm; 12 mm and 12 mm for hybrid **3i**; and 20 mm and 18 mm for the reference [16].

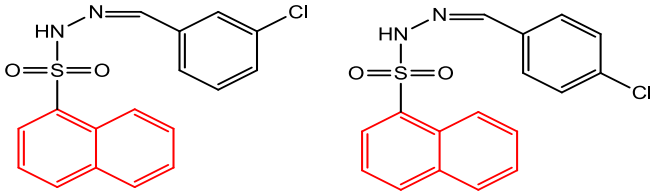
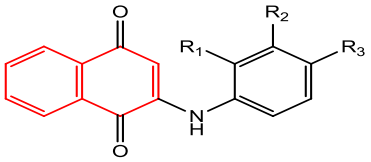


Figure 13: Albocarbons produced by Ghiya and Joshi having potent antifungal action

Ryu and his colleague have prepared three panels of albocarbon hybrids. The first is 2-arylamino-5-hydroxy-albocarbon-1,4-diones, the second involved 2-arylamino-3-chloro-5-hydroxy-albocarbon-1,4-diones, while the last panel included 3-arylamino-5-methoxy-albocarbon-1,4-diones. The antifungal activity of these hybrids was evaluated using a broth-dilution methodology and reference medicines ketoconazole and flucytosine. The employed pathogenic fungi included Candida tropicalis (C. tropicalis), Candida krusei (C. krusei), C. albicans, and A. niger were the fungal strains used in this investigation. The results revealed that the hybrids 5a-5h (Figure 14) have the best antifungal activity, with MIC values ranging from 0.8 to 12.5 g/ml. In contrast, the standard medicines had MIC values ranging from 3.2-12.5 g/ml. According to the authors of this article, the arylamine and methoxy functional groups have favorable roles in the enhanced activity of the hybrids belonging to the third panel [17].



	R_1	R_2	R_3
5a=	H	H	GH_3
5b=	H	H	Br
5c=	H	H	F
5d=	H	H	Cl
5e=	F	F	F
5f=	H	F	F
5g=	F	H	H
5h=	F	H	F

Figure 14: Chemical structures of series III hybrids produced by Ryu and his colleague

There have been numerous attempts to separate albocarbon-based products from diverse natural resources and evaluate their potential as therapeutic compounds [18-19]. Elansary *et al*. [20] isolated bis-naphthoquinone (Figure 15-a) from *Ceratostigma plumbaginoides* (Figure 15-b) as a bioactive compound and investigated its antifungal activity versus C. albicans. The isolated product had a MIC of 0.09 g/mL, which is much higher than the MICs of the standard positive controls, fluconazole and ketoconazole, which were 0.1 g/mL and 0.18 g/mL, respectively.

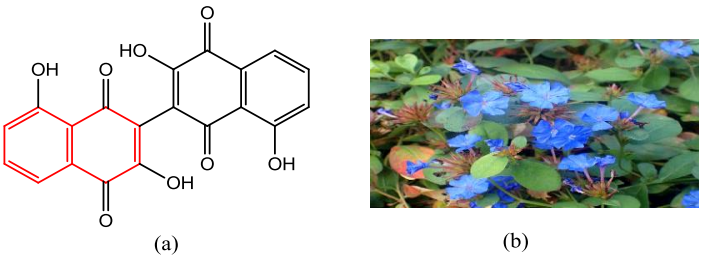


Figure 15: (a) Chemical structure of bis-naphthaquinone. (b) Ceratostigma plumbaginoides

On the other hand, the natural product (Figure 16-a) was obtained from the bark of Newbouldia laevis by grafting naphthoquinone with anthraquinone (Figure 16-b). This albocarbon-based product was tested for antifungal effectiveness against C. krusei, C. albicans, and C. glabrata. The findings demonstrated that this naturally derived product are 13 times more

efficient versus C. glabrata than the positive control, nystatin [21].

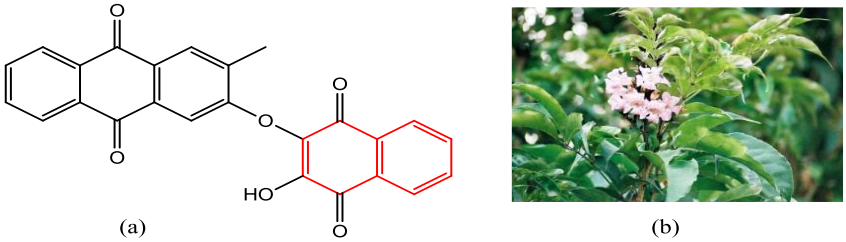


Figure 16: (a) The natural albocarbon extracted from Newbouldia laevis (b)

From Cipura paludosa bulbs (Figure 17a), Campo and his collaborators have isolated and characterized three pyranonaphthoquinones, namely eleutherol, isoeleutherine, and eleutherine. The antifungal activity of these natural agents was tested against Cryptococcus neoformans, Saccharomyces cerevisiae, C. tropicalis, and C. albicans using a broth-dilution approach. The results revealed that these compounds, notably eleutherine (Figure 17-b), have significant antifungal action. The MIC of this substance is 7.8 g/mL, compared to 0.25 g/mL for the positive control amphotericin B.

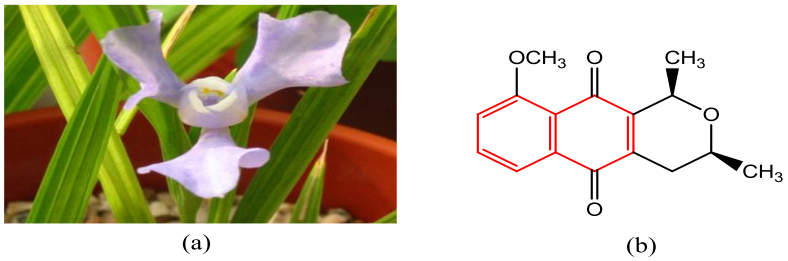


Figure 17: (a) Cipura paludosa bulb, from which the natural product eleutherine (b) was extracted

Anti-inflammatory Activity

Inflammation is a natural immunological reaction that the body uses to defend itself against tissue damage. The excessive expression of pro-inflammatory mediators (e.g., interleukin- and necrotic-mediators) and inflammatory factors (e.g., prostaglandin E2 and nitric oxide). On the other hand, inflammation may result in cell damage and, consequently, cell damage, leading to several inflammatory disorders, such as neurodegenerative diseases, arthritis, and inflammatory bowel illness [23]. As a result, the primary focus for treating inflammatory illnesses is suppressing these inflammatory factors and mediators.

The anti-inflammatory properties of albocarbon and hybrids have been extensively studied [24-29]. Muralidharan *et al*. [24] developed and characterized a new set of albocarbon-pyrimidine hybrids. Researchers employed the HRBC membrane-stabilization technique to assess their anti-inflammatory performance, which is used to discover hypotonicity-promoted RBC membrane lysis as a sensor of anti-inflammatory impact. The albocarbon-based hybrids 2a, 2c, 2d, and 2f (Figure 18) had a significant anti-inflammatory effect compared to diclofenac as a control.

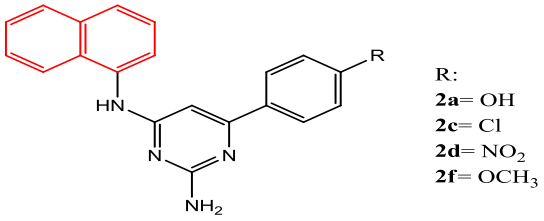


Figure 18: Albocarbons produced by Muralidharan *et al*. having an anti-inflammatory action

Naproxen is an NSAID that belongs to the propionic acid family. This member's chemical structure has an albocarbon moiety, effectively inhibiting the cyclooxygenase (COX) enzymes

resulting in pain and inflammation restriction. Several attempts have been made to lessen naproxen's GIT side effects and boost its anti-inflammatory activity. El-Husseiny *et al*. [25] studied the anti-inflammatory effects of linking several cyclic groups with naproxen-scaffold. The findings demonstrated that cyclooxygenase isozymes (COX-1 and -2) were significantly inhibited when naproxen grafted to the oxadiazoles or triazoles. Furthermore, the hybrids 6c and 10c (Figure 19) were found to have a selectivity inhibitory impact versus the COX-2 isozyme.

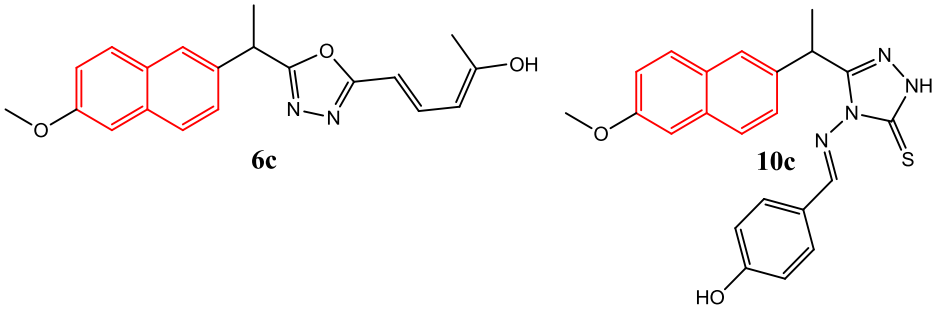


Figure 19: Naproxen hybrids synthesized by El-Husseiny *et al.*

A new series of thiazolidinone compounds grafted to albocarbon was synthesized, described, and tested for anti-inflammatory efficacy by Gangwar *et al.* When compared to diclofenac as a control. The findings indicated that two albocarbon-based hybrids, namely TB1 and TB2 (Figure 20), had a considerable anti-inflammation impact. The Carrageenan-induced paw edema methodology was used to test this effect. The paw volume after 60 min for TB1 and TB2 was 0.32 mL and 0.3 mL, respectively, compared to 0.34 mL for the reference [26].

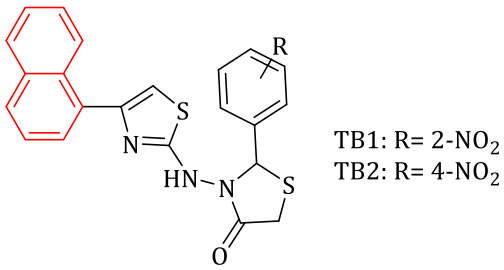


Figure 20: Backbones of TB1 and TB2 that produced via Gangwar *et al*

Albocarbons extracted from natural sources are extensively researched for their biomedical activities involving the anti-inflammatory property. Tan *et al*. distinguished seven novel spirobis-albocarbon hybrids from *Edenia gomez* pompae, a phytoendophytic fungus. To investigate if these natural hybrids had an anti-inflammatory effect, the researchers assessed nitric oxide production, as an indicator, in LPS-induced-RAW264.7 macrophagic cells. The hybrids 8 and 13 (Figure 21) displayed a solid inhibitory impact on the production of this inflammatory mediator, with IC_{50} values of 2.61 and 1.32 mol/L, respectively [27].

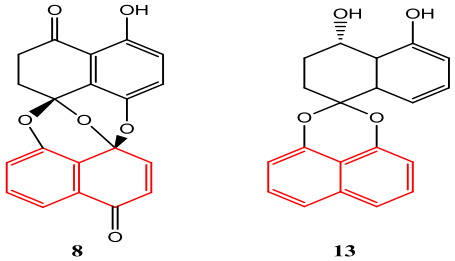


Figure 21: Albocarbons isolated from *Edenia gomez* pompae with an anti-inflammatory impact

Jin *et al*. [28] developed, identified, and tested novel albocarbon-chalcone hybrids for anti-inflammatory efficacy. The assay was performed in mice using xylene-induced ear edema and

acetic acid-induced abdominal writhing assessments. The hybrids 2f, 2i, and 2u (Figure 22) had a substantial anti-inflammatory effect, with inhibition percentages of the writhing of 58.5 %, 50.0 %, and 59.8 %, respectively. In comparison with the inhibitory percentage of indomethacin, which was employed as a standard drug.

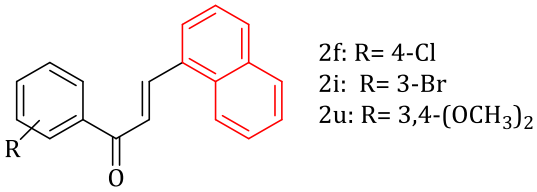


Figure 22: Chalcone-albocarbon hybrids synthesized via Jin *et al.* having potent anti-inflammatory action

Pandya *et al.* have synthesized many albocarbon-pyrazole hybrids and investigated their anti-inflammatory effects in rats using indomethacin as control and Carrageenan-induced paw edema as an investigating technique. The results revealed that the hybrids, namely 7a, 7b, 7c, and 7d (Figure 23), were substantially more effective than the standard. The hypothesized mechanism of action for these hybrids, according to the authors, is comparable to that of NSAIDs having pyrazolone ring in their structures [29].

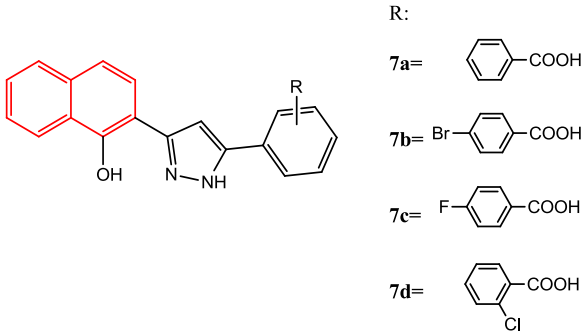


Figure 23: Albocarbons prepared via Pandya *et al*. having potent anti-inflammatory action

Antiviral Activity

Infections with pathogenic viruses account for a significant portion of infectious illnesses that impact individuals worldwide. As a result, several attempts have been made to combat such contagious viruses [30]. Albocarbon and its derivatives have been frequently exploited in developing potent antiviral medicines [31-35]. Barman *et al*. [31] used a carbohydrazide linker to bind an albocarbon-based molecule to tetrahydro albocarbon. The ability of these hybrids to block NS1, which is the abbreviation of non-structural protein 1, in the model named Madin-Darby Canine Kidney cells, was tested for anti-influenza A action. The results revealed that replacing the carbon of the linker imine with a high-ranking electron-gifting group such as cyclohexyl, or phenyl might result in a significant potentiation of activity. Consequently, hybrids with such units in their structures, such as 15 and 18 (Figure 24), have an antiviral action similar to oseltamivir.

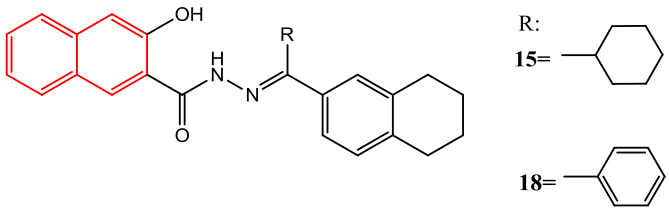


Figure 24: Albocarbons synthesized by Barman *et al*. with a potent anti-influenza virus

The stability of G-quadruplex (G4) due to HIV-1 virus growth is a potent target candidate for recently discovered antiviral medicines. Perrone *et al*. developed a novel class of molecules based

on geometric features of the specific G4 protein, which are composed of albocarbon-based derivatives welded with an aryl core. The synthesized panel's compound numbered 2 (Figure 25) displayed significant antiviral activity versus the investigated virus via a specific contact with the G4 loop. Mass spectroscopy in an electrospray ionization mode was used to track this interaction [32].

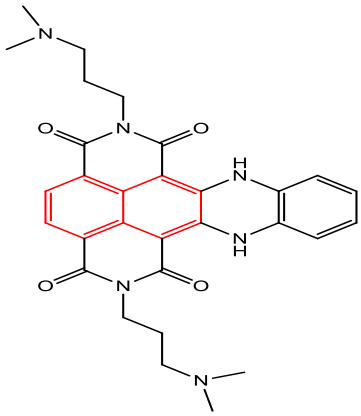
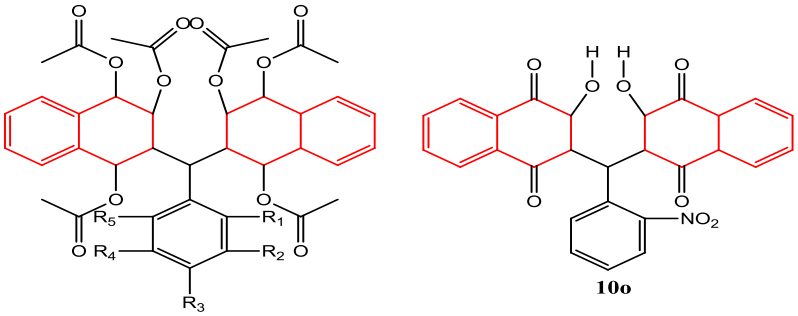


Figure 25: Albocarbon-derived product that synthesized by Perrone *et al.* [32]

Because the Zika virus may be spread to people by an infected mosquito, it poses a severe public health threat, particularly in tropical and subtropical areas. Gonzaga *et al*. [33] developed several bis-naphthoquinone-derived products and tested their anti-Zika virus activity in response to this public health concern. The EC_{50} values for five synthesized compounds, symbolized as 10o, 13e, 13h, 13j, and 13k (Figure 26), were 1.38, 0.65, 1.11, 0.62, and 0.91 M, respectively. The outcomes raise the prospect of a powerful antiviral medication to combat Zika virus infection.

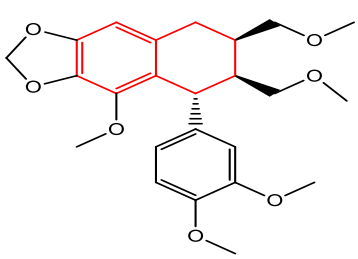


13e: $R_1=R_2=R_4=R_5=H$, $R_3=Cl$
13h: $R_1=R_2=R_4=R_5=H$, $R_3=CH_3$
13j: $R_1=R_3=R_4=R_5=H$, $R_2=OH$
13k: $R_1=R_2=R_3=R_4=R_5=F$

10o

Figure 26: Effective albocarbon-based derivatives for fighting Zika virus

Wei *et al*. [34] extracted nirtetralin-B, a new natural albocarbon from *Phyllanthus niruri* leaves (Figure 27), and investigated its potential as an anti-hepatitis B virus (HBV) candidate. According to the study findings, this product efficiently inhibited viral antigens, with IC50 values of 16.7 and 69.3 M for HBsAg and HBeAg, respectively. Furthermore, compared to acyclovir, which was employed as a control, this drug suppressed HBV at a much greater rate.



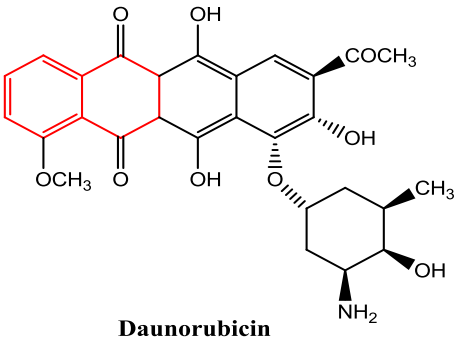
Nirtetralin-B

Phyllanthus niruri leaves

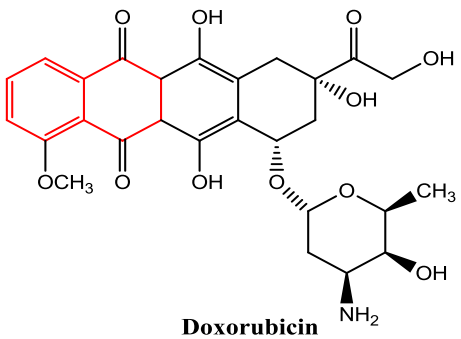
Figure 27: Chemical structure of nirtetralin-B extracted from the leaves of Phyllanthus niruri leaves

Antitumor Activity

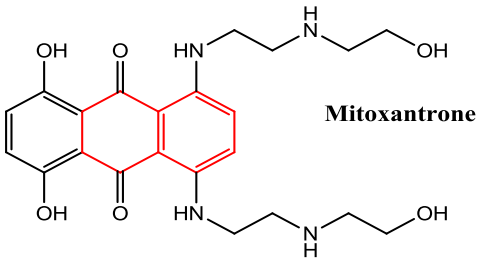
With 18.1 million diagnoses and 9.6 million deaths recorded in 2018, cancer is the second biggest cause of morbidity and mortality worldwide [35,36]. Lung, breast, and colorectal cancers are the top three cancer phenotypes in mortality incidence [37,38]. Many attempts have been made to rehabilitate humanity's stock to combat this form of fatal sickness [39-47]. Many synthetic chemicals have been produced and tested against many types of cancer, including albocarbon and its derivatives. For example, daunorubicin, doxorubicin, and mitoxantrone are natural cytotoxic medicines with naphthoquinone as their fundamental component (Figure 28). These tumor-killing natural assassins blocked DNA topoisomerase I and II, resulting in apoptosis [39].



Daunorubicin



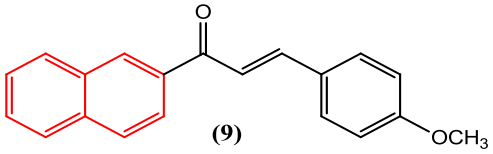
Doxorubicin



Mitoxantrone

Figure 28: Chemical structures of the albocarbon-anticancer hybrids

Budhiraja *et al.* created a series of albocarbon-chalcone hybrids with a functionalized aryl moeity linked to them. The resulting hybrids were investigated as cytotoxic applicants against malignant cell lines from the neuroblastoma (IMR-32), ovarian (OVACAR), prostate (PC-3), and liver (HEP-2). The results showed that compound **9** (Figure 29) had the decisive action, with inhibition percentages of 81, 88, 75, and 72, respectively, against the abovementioned cell lines.



(9)

Figure 29: Compound numbered 9 produced by Budhiraja *et al.*

By hybridizing albocarbon with butyrolactone-based products, Rajabi *et al.* have created a variety of hybrids. The resulting derivatives were tested *in vitro* against the malignant cell lines MCF-7 (breast) and HCT-15 (colon). The hybrid **4** (Figure 30) was the most effective against the applied cancerous-line cells, with IC_{50} values extending from 64 to 66 M [41].

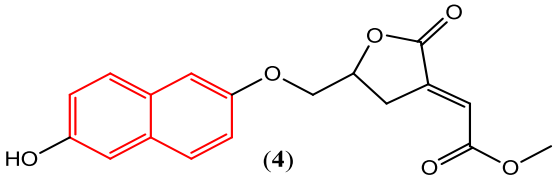


Figure 30: Conjugate numbered 4produced by Rajabi *et al.*

Spaczyska *et al.* developed and synthesized several albocarbon-based hybrids, which they then investigated for cytotoxicity in human colon cancer cell lines *in vitro*. The hybrids (Figure 31) with Cl, Br, CF_3, NO_2, or OCH_3 substituents had the most significant effects, with IC_{50} values ranging from 6.25 to 25 M, compared to the IC_{50} of 5-fluorouracil, which was 4.42 M. The intercalation of these hybrids with DNA, according to the author, might be a plausible mechanism of action [42].

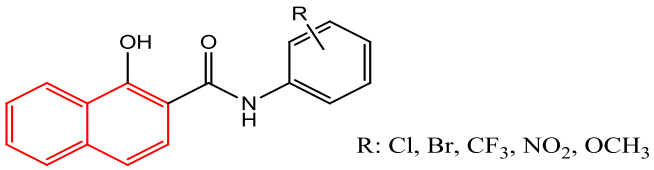


Figure 31: Chemical structures of the effective 1-hydroxyalbocarbon-2-carboxamides

Karakurt *et al.* developed a novel panel of albocarbon-pyrazole hybrids. Using mouse fibroblast and human neuroblastoma cell lines, the toxicity impact of these hybrids was studied *in vitro*. The results depicted that most of the produced compounds had inhibitory ratios between 505 and 60% toward the investigated cancerous lines, with no detectable effect on the normal fibroblasts. Furthermore, 7a (Figure 32) was the most potent hybrid among the synthesized hybrids with an IC_{50} value of 85.94 M compared to vincristine, which had an IC_{50} value of 25.46 M [43].

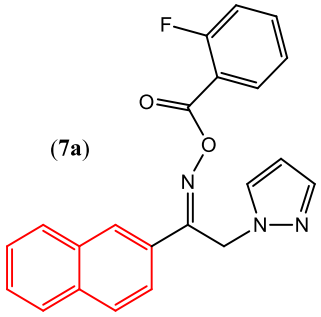


Figure 32: Chemical backbone of the albocarbon hybrid named 7a

Yuan *et al.* synthesized various albocarbon-thiazole-pyrazole hybrids and assessed their toxicity versus the HeLa cell line. The hybrid 7d (Figure 33) was shown to be the most efficacious, with an IC_{50} value of 0.12 M, in comparison with a recently developed cytotoxic drug named gefitinib, which had an IC_{50} value of 2.67 M. The cytotoxic impact of this hybrid was shown to be closely connected to the substitution on ring A in the SAR investigation. Furthermore, the docking simulation revealed that the targeted conjugate's Albocarbon ring could establish two pi-bonds with LYS721 of the EGFR (overexpression receptor) active site, which might explain the conjugate's high activity [44].

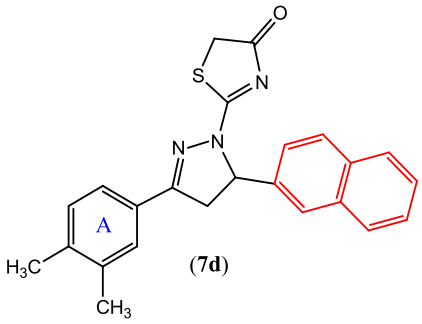


Figure 33: Chemical backbone of the albocarbon-derived compound named 7d

A panel of glycosidic naphthoquinones was synthesized and assessed for *in vitro* cytotoxicity toward a *mouse Ehrlich carcinoma* cell line. The glycosylated naphthoquinones were found to be highly potent, with conjugate **42** being the best with an IC_{50} of 5.1 M compared to cisplatin's IC_{50} of 50.1 M as a standard cytotoxic drug. These findings suggested that glycosylation significantly impacts the cytotoxic capacity of the glycosylated derivatives compared with the corresponding parent compounds [45].

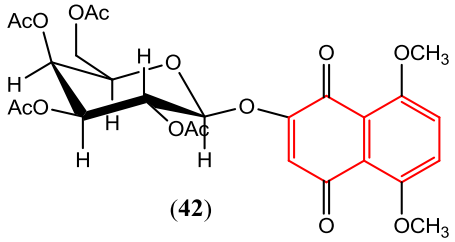


Figure 34: Chemical structure of the glycosylated naphthoquinone [42]

Wang *et al.* synthesized several albocarbon-based compounds grafted to the indole heterocycle using a chalcone linker. The hybrids' *in vitro* cytotoxicity was tested against three human malignant cell lines: breast adenocarcinoma (MCF-7), hepatocellular carcinoma (HEPG2), and colon carcinoma (HCT116). The conjugate designated as 7 (Figure 35) was the most efficient against HCT116, HEPG2, and MCF-7, with IC_{50} values of 1.13, 0.65, and 0.82 M, respectively. The capacity of this compound to impede tubulin polymerization and consequently block the G_2/M phase of the cell cycle was discovered in a mechanism investigation [46].

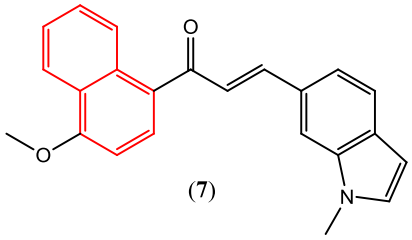


Figure 35: Chemical backbone of the conjugate designated as 7 produced by Wang *et al.* [46]

Altintop *et al.* produced several albocarbon-based semicarbazones and tested their cytotoxicity against human prostate cancer cells *in vitro* (LNCaP). The hybrid designated as 6 with an aryl functionality (Figure 36) was the best among the other hybrids, inhibiting up to 83 % of the tumor cells [47].

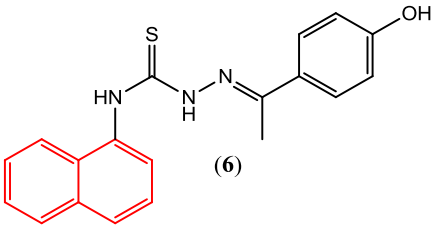


Figure 36: Chemical backbone of the albocarbon-based compound designated as 6

Free Radicals Quenching Activity

The oxidative stress caused by high quantities of harmful free radicals has been linked to various human disorders, including stroke, atherosclerosis, ischemic heart disease, cancer, and inflammation [48,49]. Free radicals, such as superoxide anion, reactive oxygen species (ROS), nitric oxide and peroxyl radicals, can interact with lipids, proteins, and DNA, resulting in various health concerns [50,51]. Trapping free radicals has been a popular research topic to preserve the healthy tissues from potentially detrimental effects [52].

Ateş-Alagöz *et al.* created many 5-substituted-6-fluorobenzimidazole derivatives, in which the 1,2,3,4-tetrahydroalbocarbon-1,1,4,4-tetramethyl entity was hybridized with the benzimidazole ring's position 2. At 10-3 M concentrations, all the produced compounds had strong superoxide scavenging action. Furthermore, compared to the quenching enzyme superoxide dismutase, which had a quenching impact of 76 % [53], hybrid **5** (Figure 37) had the most significant trapping capacity, reaching 98 %.

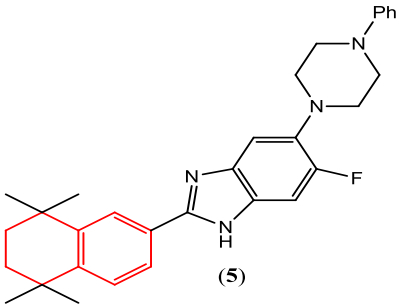


Figure 37: Chemical structure of the albocarbon-based hybrid named 5

By substituting the indole ring with albocarbon rings of different aromatic-substituted side chains, Shirinzadeh *et al.* have synthesized and created numerous melatonin bioisosteres (Figure 38). The radical trapping activity of the produced compounds was tested *in vitro*. According to the study, these compounds were shown to be extremely potent antioxidant agents. The authors attribute the enhanced activity to the lack of the 6-methoxy group and the substitution of the indole ring with that of albocarbon [54].

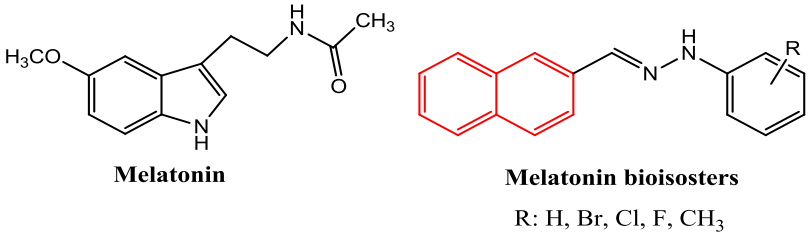


Figure 38: Structural framework of the melatonin and its generated isostere

Hamdy *et al.* synthesized many albocarbon-pyrazolo pyridine hybrids and tested their quenching capability using a DPPH experiment with ascorbic acid as a control. The results revealed that the hybrid symbolized as 5a (Figure 39) performed better as an antioxidant applicant than the other synthesized hybrids and standard [55].

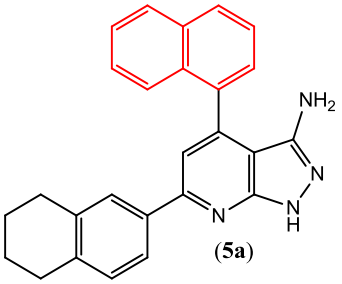


Figure 39: Structural backbone of the hybrid designated as 5a

Somashekara B *et al.* produced several albocarbon-imidazole hybrids and used a DPPH-radical scavenging experiment to test their antioxidant ability. Compared to the control, butylated hydroxyanisole (BHA), the hybrids 2d, 2g, and 2K (Figure 40) demonstrated high quenching capability. According to the research, the enhanced activity was attributed to the albocarbon moiety and the replacement of excellent electron-donating groups on locations 5 and 4 of the imidazole heterocyclic ring [56].

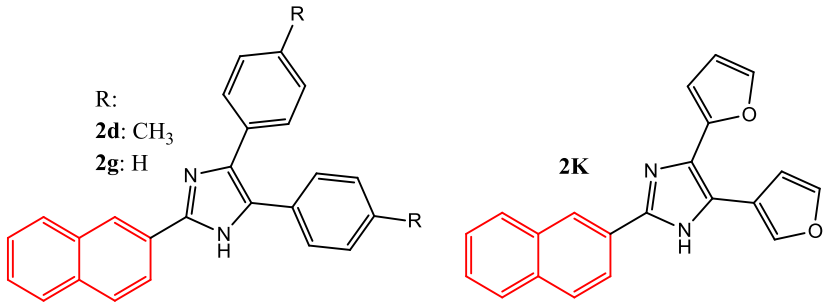


Figure 40: Albocarbon-imidazole hybrids produced via Somashekara B *et al.*

Wadhwa D *et al.* [57] synthesized a new series of albocarbons hybridized with (*E*)2,3-dihydrofuro[3,2-c] coumarin and investigated the *in vitro* antiradical potential utilizing an H_2O_2-trapping assay. Compared to BHA, all produced compounds had equivalent antiradical activity. Furthermore, even at the lowest concentration (10 M/ml), the compound designated 4f (Figure 41) demonstrated the best effect compared to the control. The inclusion of an electron-withdrawing entity on the aryl functionality hybridized with a dihydro-furan ring, according to the authors, may increase the antiradical activity of such compounds.

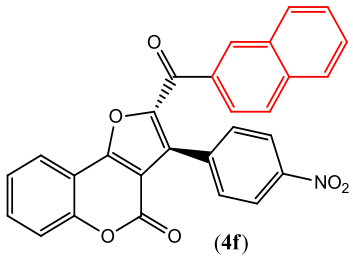


Figure 41: Chemical backbone of the albocarbon linked with dihydrofurocoumarin (4f)

Gouda *et al.* [58] produced several benzothiophene-naphthoquinone hybrids and tested their antioxidative activity *in vitro* using the ABTS-screening assay. The hybrid known as 9a (Figure 42) was shown to be the most effective, with a 95.97 inhibitory percentage compared to 89.87% for ascorbic acid. In addition, this research found that these produced hybrids may protect DNA against the toxic agent bleomycin.

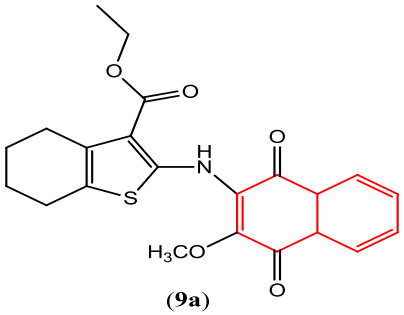


Figure 42: The chemical backbone of the albocarbon-based compound designated as termed 9a

Ozen *et al*. [72] created a Schiff-base linker in twelve albocarbon-based compounds. Several techniques were used to test these hybrids' free radical scavenging capability, including metal chelating, phosphomolybdenum, reducing power, lipid peroxidation, and H_2O_2 scavenging activity experiments [59-71]. Compared to the control, the hybrids symbolized as NAPH5, NAPH10, and NAPH12 (Figure 43) were the most effective antioxidants at 10 and 50 mM doses. The findings of this study might pave the way for the development of potent antioxidants for medical and industrial applications.

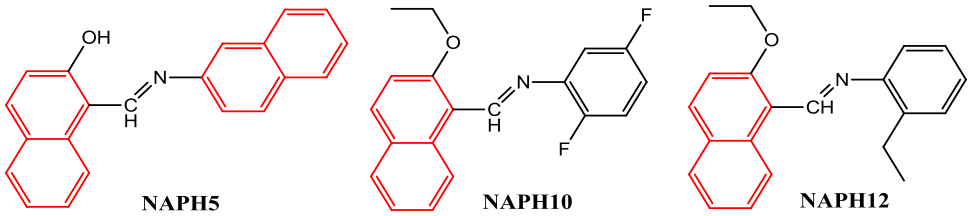


Figure 43: Albocarbons with imine linkage that having a potent antiradical activity

Albocarbon compounds, antioxidants, herbal and fungal active ingredients are micro-pharmaceutical compounds that can exert a wide range of medicinal effects such as antimicrobial, antioxidant, and anti-inflammatory properties [73-83].

Conclusions

The hybridizing of albocarbon-based compounds to the different cyclic moieties has been a common theme in searching for novel lead compounds in various pharmacological domains. According to the studies mentioned above, this hybridization improved various pharmacological activities of the synthesized hybrids compared to the corresponding parent albocarbons. The authors concluded that his finding might contribute to the hybrids' increased lipophilicity. By creating additional Van der Waals forces, this property might boost the insight of these hybrids into their targeted cells and strengthen the generated drug-target interactions.

Acknowledgments: The authors are very grateful to the University of Mosul/College of Pharmacy for their provided facilities, which helped to improve the quality of this work.

Financial Support: The work is totally self-funded.

Authors' contributions: The authors are equally contributed in this work.

Conflict of Interest: There are no conflicts of interest.

ORCID:

Yasser Fakri Mustafa:
https://www.orcid.org/0000-0002-0926-7428
Moath Kahtan Bashir:
https://www.orcid.org/0000-0003-3403-341X
Mahmood Khudhayer Oglah:
https://www.orcid.org/0000-0001-8616-154X

References

[1]. Rokade Y.B., Sayyed R.Z., *Rasayan J. Chem.*, 2009, **42** [Crossref], [Google Scholar], [Publisher]
[2]. Oglah M.K., Mustafa Y.F., Bashir M.K., Jasim M.H., *Sys. Rev. Pharm.*, 2020, **11**:472 [Crossref], [Google Scholar], [Publisher]
[3]. Bashir M.K., Mustafa Y.F., Oglah M.K., *Period. Tche Quimica*, 2020, **17**:871 [Google Scholar], [Publisher]
[4]. Mustafa Y.F., Khalil R.R., Mohammed E.T., *Sys. Rev. Pharm.*, 2020, **11**:382 [Google Scholar], [Publisher]
[5]. Mustafa Y.F., Mohammed E.T., Khalil R.R., *Egypt. J. Chem.*, 2021, **64**:4461 [Crossref], [Google Scholar], [Publisher]
[6]. Mohammed E.T., Mustafa Y.F., *Sys. Rev. Pharm.*, 2020, **11**:64 [Google Scholar], [Publisher]
[7]. Ashraf K., Yasrebi K., Adeniyi E.T., Hertlein T., Ohlsen K., Lalk M., Erdmann F., Hilgeroth A., *Drug Des. Devel. Ther.*, 2019, **13**:275 [Crossref], [Google Scholar], [Publisher]

[8]. Chopra B., Dhingra A.K., Kapoor R.P., Parsad D.N., *J. Explor. Res. Pharmacol.*, 2017, **2**:105 [Crossref], [Google Scholar], [Publisher]
[9]. Sivasankari S., Mary M.R., *World News Nat. Sci.*, 2018, **18**:124 [Google Scholar], [Publisher]
[10]. Kumar R.K., Sharma R.S.K., Kumar D.R., Havale S.H., Basaveswararao B., Murali S.V., *Der Pharma Chem.*, 2016, **8**:374 [Google Scholar], [Publisher]
[11]. Zangade S.B., Jadhav J.D., Lalpod, Vibhute Y.B., Dawane B.S., *J. Chem. Pharm. Res.*, 2010, **2**:310 [Google Scholar], [Publisher]
[12]. Azarifar D., Shaebanzadeh M., *Molecules*, 2002, **7**:885 [Crossref], [Google Scholar], [Publisher]
[13]. Kara E.M., Jannuzzi A.T., Bayrak N., Yildirim H., Yildiz M., Tuyun A.F., Alpertunga B., Celik B.O., *Eur. J. Biol.*, 2019, **78**:117 [Crossref], [Google Scholar], [Publisher]
[14]. Shakh Y.U., Romanenko I., Slesarchuk M., Syngaevsky V., Kovalchuk O., Bolibrukh K., Karkhut A., Bolibrukh L., Gubytska I., Komarovska-Porokhnyavets O., Polovkovych S., *Indian J. Pharm. Sci.*, 2017, **79**:650 [Crossref], [Google Scholar], [Publisher]
[15]. Patel M., Patel K., *Heterocycl. Comm.*, 2019, **25**:146 [Crossref], [Google Scholar], [Publisher]
[16]. Ghiya S., Joshi Y.C., *Int. J. Pharm. Pharm. Sci.*, 2015, **7**:249 [Publisher]
[17]. Ryu C-K., Chae M.J., *Arch. Pharm. Res.*, 2005, **28**:750 [Crossref], [Google Scholar], [Publisher]
[18]. Mustafa Y.F., Abdulaziz N.T., *Sys. Rev. Pharm.*, 2020, **11**:438 [Google Scholar], [Publisher]
[19]. Mustafa Y.F., Bashir M.K., and Oglah M.K. *Sys. Rev. Pharm.*, 2020, **11**:598 [Google Scholar], [Publisher]
[20]. Elansary H.O., Yessoufou K., Mahmoud E.A., Skalicka-Woźniake K., *Nat. Prod. Commun.*, 2016, **11**:1455 [Crossref], [Google Scholar], [Publisher]
[21]. Eyong K.O., Folefoc G.N., Kuete V., Beng V.P., Krohu K., Hussain H., Nkengfack A.E., Saeftel M., Sarite S.R., Hoerauf A., *Phytochemistry*, 2006, **67**:605 [Crossref], [Google Scholar], [Publisher]
[22]. Campos A., Souza G.M.P., Monache F.D., Butassi E., Zacchino S., Filho V.C., *Nat. Prod. Commun.*, 2015, **10**:1589 [Crossref], [Google Scholar], [Publisher]
[23]. Mustafa Y.F., Oglah M.K., Bashir M.K., *Sys. Rev. Pharm.*, 2020, **11**:482 [Google Scholar], [Publisher]
[24].Tao B., Ye F., Li H., Hu Q., Xue S., Zhao G. *J. Agric. Food Chem.,* 2014, **62**:7166 [Crossref] [Google Scholar] [Publisher]
[25]. El-Husseiny W.M., El-Sayed M.A., Abdel-Aziz N.I., El-Azab A.S., Asiri Y.A., Abdel-Aziz A.A., *Eur. J. Med. Chem.*, 2018, **158**:134 [Crossref], [Google Scholar], [Publisher]
[26]. Gangwar P., Sharma P., Shrivastava B., Sharma J., Sharma S., *Int. J. Curr. Trends Pharm. Res.*, 2013, **1**:181 [Google Scholar], [Publisher]
[27]. Tan Y., Guo Z., Zhu M., Shi J., Li W., Jiao R., Tan R., Ge H., *Chin. Chem. Lett.*, 2020, **31**:1406 [Crossref], [Google Scholar], [Publisher]
[28]. Jin Q.H., Chen H.H., Chen W.B., Fu Z.Y., Guan L.P., Jiang H.Y., *Med. Chem. Res.*, 2020, **29**:877 [Crossref], [Google Scholar], [Publisher]
[29]. Pandya A.B., Prajapti D.G., Pandya S.S., *J. App. Pharm. Sci.*, 2012, **2**:226 [Crossref], [Google Scholar], [Publisher]
[30]. Oglah M.K., Bashir M.K., Mustafa Y.F., Mohammed E.T., Riyadh R., *Sys. Rev. Pharm.*, 2020, **11**:717 [Google Scholar], [Publisher]
[31]. Barman S., You L., Chen R., Codrea V., Kago G., Edupuganti R., Robertus J., Krug R.M., Anslyn E.V., *Eur. J. Med. Chem.*, 2014, **71**:81 [Crossref], [Google Scholar], [Publisher]
[32]. Perrone R., Doria F., Butovskaya E., Frasson I., Botti S., Scalabrin M., Lago S., Grande V., Nadai M., Freccero M., Richter S.N., *J. Med. Chem.*, 2015, **58**:9639 [Crossref], [Google Scholar], [Publisher]
[33]. Gonzaga D.T.G., Gomes R.S.P., Marra R.K.F., Da Silva F.C., Gomes M.W.L., Ferreira D.F., *et al. J. Braz. Chem. Soc.*, 2019, **30**:1697 [Crossref], [Google Scholar], [Publisher]
[34]. Wei W., Li X., Wang K., Zhang Z., Zhou M., *Phytother. Res.*, 2012, **26**:964 [Crossref], [Google Scholar], [Publisher]
[35]. Oglah M.K., Mustafa Y.F., *J. Glob. Pharma Technol.*, 2020, **12**:854 [Google Scholar], [Publisher]
[36]. Mustafa Y.F., *J. Med. Chem. Sci.*, 2021, **4**:612 [Crossref], [Google Scholar], [Publisher]
[37]. Bray F., Ferlay J., Soerjomataram I., Siegel R.L., Torre L.A., Jemal A., *A Cancer J. Clin.*, 2018, **68**:394 [Crossref], [Google Scholar], [Publisher]

[38]. Bashir M.K., Mustafa Y.F., Oglah M.K., *Sys. Rev. Pharm.*, 2020, **11**:175 [Google Scholar], [Publisher]
[39]. Pereyra C.E., Dantas R.F., Ferreira S.B., Gomes L.P., Silva-Jr F.P., *Cancer Cell Int.*, 2019, **19**:207 [Crossref], [Google Scholar], [Publisher]
[40]. Budhiraja A., Kadian K., Kuar M., Aggarwal V., Gafg A., Sapra S., Nepali K., Suri O.P., Dhar K.L., *Med. Chem. Res.*, 2012, **21**:2133 [Crossref], [Google Scholar], [Publisher]
[41]. Rajabi M., Khalilzadeh M.A., Tavakolinia F., Signorelli P., Ghidoni R., Santaniello E., *DNA Cell Biol.*, 2012, **31**:783 [Crossref], [Google Scholar], [Publisher]
[42]. Spaczyńska E., Mrozek-Wilczkiewicz A., Malarz K., Kos J., Gonec T., Oravec M., Gawecki R., Bak A., Dohanosova J., Kapustikova I., Liptaj T., *Scientific Reports*, 2019, **9**:1 [Crossref], [Google Scholar], [Publisher]
[43]. Karakurt A., Bozbey I., Uslu H., Sari S., Özdemir Z., Şalva E., *Trop. J. Pharm. Res.*, 2019, **18**:1315 [Crossref], [Google Scholar], [Publisher]
[44]. Yuan J.W., Wang S.F., Luo Z.L., Qiu H.Y., Wang P.F., Zhang X., Yang Y.A., Yin Y., Zhang F., Zhu H.L., *Bioorganic Med. Chem. Lett.*, 2014, **24**:2324 [Crossref], [Google Scholar], [Publisher]
[45]. Sabutski Y.E., Semenova M.N., Yurchenko E.A., Polonik N.S., Denisenko V.A., Dmitrenok P.S., Semenov V.V., Polonik S.G., *Nat. Prod. Commun.*, 2017, **12**:1081 [Crossref], [Google Scholar], [Publisher]
[46]. Wang G., Peng Z., Li Y., *Chem. Pharm. Bull.*, 2019, **67**:725 [Crossref], [Google Scholar], [Publisher]
[47]. Altintop M.O., Sever B., Özdemir A., Kuş G., Oztopcu-Vatan P., Kabadere S., *Kaplancikli* Z.A., *J. Enzyme Inhib. Med. Chem.*, 2015, **31**:410 [Crossref], [Google Scholar], [Publisher]
[48]. Khalil R.R., Mustafa Y.F., *Syst. Rev. Pharm.*, 2020, **11**:57 [Google Scholar], [Publisher]
[49]. Mustafa Y.F., Mohammed E.T., Khalil R.R. *Sys. Rev. Pharm.*, 2020, **11**:570 [Google Scholar], [Publisher]
[50]. Mustafa Y.F., *J. Glob. Pharma Technol.*, 2019, **11**:1 [Google Scholar], [Publisher]
[51]. Mustafa Y.F., Najem M.A., Tawffiq Z.S., *J. App. Pharm. Sci.*, 2018, **8**:49 [Crossref], [Google Scholar], [Publisher]
[52]. Lobo V., Patil A., Phatak A., Chandra N., *Pharmacogn. Rev.*, 2010, **4**:118 [Crossref], [Google Scholar], [Publisher]
[53]. Ateş-alagöz Z., Kuş C., Çoban T., *J. Enzyme Inhib. Med. Chem.*, 2005, **20**:325 [Crossref], [Google Scholar], [Publisher]
[54]. Shirinzadeh H., Ghalia M., Tascioglu A., Adjali F.I., Gunesacar G., Gurer-Orhan H., Suzen S., *Braz. J. Pharm. Sci.*, 2020, **56**:1 [Crossref], [Google Scholar], [Publisher]
[55]. Hamdy N.A., Anwar M.M., Abu-Zied K.M., Awad H.M., *Acta Pol. Pharmaceutica - Drug Res.*, 2013, **70**:987 [Google Scholar], [Publisher]
[56]. Somashekara B., Thippeswamy B., Vigayakumar G.R., *J. Chem. Sci.*, 2019, **131**:1 [Crossref], [Google Scholar], [Publisher]
[57]. Wadhwa D., Arora V., Arora L., Arora P., Parkash O., *J. Heterocycl. Chem.*, 2015, **53**:1030 [Crossref], [Google Scholar], [Publisher]
[58]. Gouda M.A., Eldien H.F., Girges M.M., Berghot M.A., *Med. Chem.*, 2013, **3**:2228 [Crossref], [Google Scholar], [Publisher]
[59]. Mustafa Y.F., Abdulaziz N.T., Jasim M.H., *Egypt. J. Chem.*, 2021, **64**:1807 [Crossref], [Google Scholar], [Publisher] (
[60]. Nejres A.M., Mustafa Y.F., Aldewachi H.S., *Int. J. Pavement Eng.*, 2022, **23**:39 [Crossref], [Google Scholar], [Publisher]
[61]. Nejres A.M., Ali H.K., Behnam S.P., Mustafa Y.F. *Syst. Rev. Pharm.*, 2020, **11**:726 [Google Scholar], [Publisher]
[62]. Mustafa Y.F., Khalil R.R., Mohammed E.T., Bashir M.K., Oglah M.K. *Arch. Razi Inst.*, 2021, **76**:1297 [Crossref], [Google Scholar], [Publisher]
[63].Aldewachi H., Mustafa Y.F., Najm R., Ammar F., *Sys. Rev. Pharm.*, 2020, **11**:289 [Crossref], [Google Scholar], [Publisher]
[64]. Mustafa Y.F., Bashir M.K., Oglah M.K., Khalil R.R., Mohammed E.T., *NeuroQuantology*, 2021, **19**:129 [Crossref], [Google Scholar], [Publisher]
[65]. Mustafa Y.F., Abdulaziz N.T., *NeuroQuantology*, 2021, **19**:175 [Crossref], [Google Scholar], [Publisher] (Google Scholar)
[66]. Mustafa Y.F., Mohammed N.A., *Biochem. Cell. Arch.*, 2021, **21**:1991 [Google Scholar], [Publisher]

[67]. Mustafa Y.F., Khalil R.R., Mohammed E.T., *Egypt. J. Chem.*, 2021, **64**:3711 [Crossref], [Google Scholar], [Publisher]
[68]. Mustafa, Y.F., *NeuroQuantology*, 2021, **19**:99 [Crossref], [Google Scholar], [Publisher]
[69]. Mustafa Y.F., *Appl. Nanosci.*, 2021 [Crossref], [Google Scholar], [Publisher]
[70]. Mustafa Y.F., Kasim S.M., Al.Dabbagh B.M., Al.Shakarchi W., *Appl. Nanosci.*, 2021 [Crossref], [Google Scholar], [Publisher]
[71]. Mahmood A.A.J., Mustafa Y.F., Abdulstaar M., *Int. Med. J. Malays.*, 2014, **13**:3 [Crossref], [Google Scholar], [Publisher]
[72]. Ozen T., Macit M., Toka M., *Journal Sains Kesihatan Malaysia*, 2018, **16**:45 [Crossref]
[73].Wani N.A., Khanday W.I., Tirumale S., *J. Nat. Sci. Biol. Med.*, 2020, **11**:72 [Crossref], [Google Scholar], [Publisher]
[74]. Ramesh C., Vinithkumar N.V., Kirubagaran R., *J. Nat. Sci. Biol. Med.*, 2019, **10**:104 [Crossref], [Google Scholar], [Publisher]
[75]. Džambić A., Muratović S., Veljović E., Softić A., Dautović E., Husejnović M.Š., Smajlović A., *Eur. Chem. Bull.*, 2020, **9**:285 [Google Scholar], [Publisher]
[76]. Bhale S.P., Yadav A.R., Pathare P.G., Tekale S.U., Franguelli F.P., Kótai L., Pawar R.P., *Eur. Chem. Bull.*, 2020, **9**:430 [Google Scholar], [Publisher]
Muluk M.B., Patil P.S., Kasare S.L., Kulkarni R.S., Dixit P.P., Choudhari P.B., Haval K.P., *Eur. Chem. Bull.*, 2020, **9**:184 [Google Scholar], [Publisher]
[77].Mojtabavi L., Razavi A., *Eur. Chem. Bull.*, 2020, **9**:1 [Crossref], [Google Scholar], [Publisher]
[78].Halim S., Mohamad N., Ridzuan P.M., Zakaria N.H., Muhammad N.A., *IIUM Med. J. Malays.*, 2019, **18**:47 [Crossref], [Google Scholar], [Publisher]
[79].Wan A.E., Khan M.S.B., Teo B.S.X., Khan J., Abdullah I., Kaleemullah M., Rasny M.R.M., *Int. J. Med. Toxicol. Leg. Med.*, 2020, **23**:169 [Crossref], [Google Scholar], [Publisher]
[80].Khan J., Kusmahani S.H., Ruhi S., Al-Dhalli S., Kaleemullah M., Saad R., Yusuf E., *Int. J. Med. Toxicol. Leg. Med.*, 2020, **23**:149 [Google Scholar], [Publisher]
[81].Al-Shawi S.G., Andreevna Alekhina N., Aravindhan S., Thangavelu L., Elena A., Viktorovna Kartamysheva N., Rafkatovna Zakieva R., *J. Nanostruct.*, 2021, **11**:181 [Crossref], [Google Scholar], [Publisher]
[82].Magbool F.F., Ibrahim Elnima E., Shayoub M.E., Hamedelniel E.I., Gamil A.M., Adam M.E., Osman Z., *Plant Biotechnol. Persa*, 2020, **2**:1 [Crossref], [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE
Yasser Fakri Mustafa, Moath Kahtan Bashir, Mahmood Khudhayer Oglah. Influence of Albocarbon-cyclic Hybridization on Biomedical Activities: A review, *J. Med. Chem. Sci.*, 2022, 5(4) 518-536
DOI: 10.26655/JMCHEMSCI.2022.4.8
URL: http://www.jmchemsci.com/article_143662.html