

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Research on Natural Phenolic Compounds in FAB-Lab: Nonconventional Industrial, Pharmaceutical, and Therapeutic Applications

Farid A. Badria

Abstract

Phenolic compounds represent one of the secondary metabolites of plants with pharmaceutical and therapeutic applications. Flavonoids, quinones, bioflavonoids, neolignans, xanthonoids, curcuminoids, tannins, and coumarins are some examples of the major groups of commonly available phenolic compounds in our daily foods, beverages, and spices. From this standpoint, the Liver Research Laboratory (FAB Lab) at Mansoura university, Egypt, established a multidisciplinary research (chemistry, molecular biology, bioinformatics, pharmacology, and pharmaceuticals) based on utilization of commonly abundant natural products from plants and agricultural wastes, especially phenolic compounds to meet the goal of applied scientific research in pharmaceutical industry, environment, public health, and to furnish a sustainable well-developed globe. Examples of our concerted efforts, for over 30 years, are in the area of natural products and utilization of environmental waste containing phenolic compounds for various health disorders (cancer, cataract, degenerative diseases, hyperpigmentation, hyperglycemia, skin disorders), nano-, green and click chemistry. This chapter presents a practical model from FAB-Lab to maximize the benefits from phenolic natural products that have not been optimally exploited to establish meaningful scientific applied research. Patents, innovations, and significant publications indexed by the Web of Science and Scopus databases in the journals that occupy the 1st and the 2nd quartile will be presented.

Keywords: phenolic compounds, green chemistry, environment-friendly industry, therapeutic applications

1. Introduction

The Liver Research Laboratory (FAB-Lab) was established in 1990 in the Department of Pharmacognosy, Faculty of Pharmacy, Mansoura University, Egypt. FAB-Lab adopts various research projects aimed at innovation in health, environmental, and pharmaceutical industry issues.

To reach today's destination, FAB-Lab based the ongoing research on the following premises:

1. A sound healthy environment embraces a sound and healthy society.
2. A healthy environment provides us with a cure to any ailment.
3. An unhealthy environment is the source of all illnesses.

2. Vision and mission of FAB-Lab

The Liver Research Laboratory (FAB-Lab) was established in 1990 in the Department of Pharmacognosy, Faculty of Pharmacy, Mansoura University, Egypt. FAB-Lab adopts various research projects aimed at innovation in health, environmental, and pharmaceutical industry issues.

Vision: Conducting distinguished research in the field of drug discoveries from natural sources with tangible returns at the regional and international levels.

Message: FAB-Lab seeks to promote integration between different departments in the field of drug discovery to contribute in solving health problems.

The research strategy depends on shifting from conventional approaches in medicine (treating symptoms) to a more holistic approach that is patient/environment-centered.

The drug discovery team, Badria and coworkers, at Pharmacognosy department, Mansoura University presented many significant contributions in using simple, economic, and abundantly available phenolic compounds to produce a series of useful analogues that exhibited very promising applications industrial and therapeutic applications (as shown in **Figure 1**).

One of FAB-Lab's early papers entitled "Is Man Helpless Against Cancer: An Environmental Approach in "Cancer Letters" in 1994 [1] is a landmark in exploiting the role of foods, medicinal plants, and herbs rich in phenolic compounds in prophylaxis and treatment of cancer.

FAB-Lab stressed the role of green and conventional chemistry using natural, in-house resources and facilities as friendly environmental substances to construct new therapeutic agents for the well-being of society; e.g., for treatment of epidemics of neglected tropical diseases such as Schistosomiasis [2]. The extensive studies on environment-friendly chemistry revealed valuable information about the root cause of many complex health disorders. Therefore, a final highlight is considered a serious attempt toward solving local, regional, and global problem via designing and producing a drug from agricultural wastes, foods, and plants for treatment of cancer and hepatic disorders [3–9], degenerative diseases [10, 11], hair and skin [12], dentistry [13], ophthalmology [14], breast cancer [15–20], osteoarthritis [21], and bronchial asthma [22, 23].

Liver research laboratory (FAB-Lab, Faculty of Pharmacy, Mansoura University, Mansoura, Egypt) presented a multidisciplinary approach for nonconventional industrial, pharmaceutical, and therapeutic applications.

These efforts demonstrate that, despite the many limitations of NPs, reasonable modifications may lead to the discovery of a novel drug. From this standpoint, the Liver Research Laboratory (FAB Lab) was a pioneer in designing a system to meet the goal of the scientific research in order to serve society, the environment, public health, and to furnish a sustainable well-developed globe. Examples of our concerted efforts, for over 30 years, are in the area of natural products and utilization of environmental

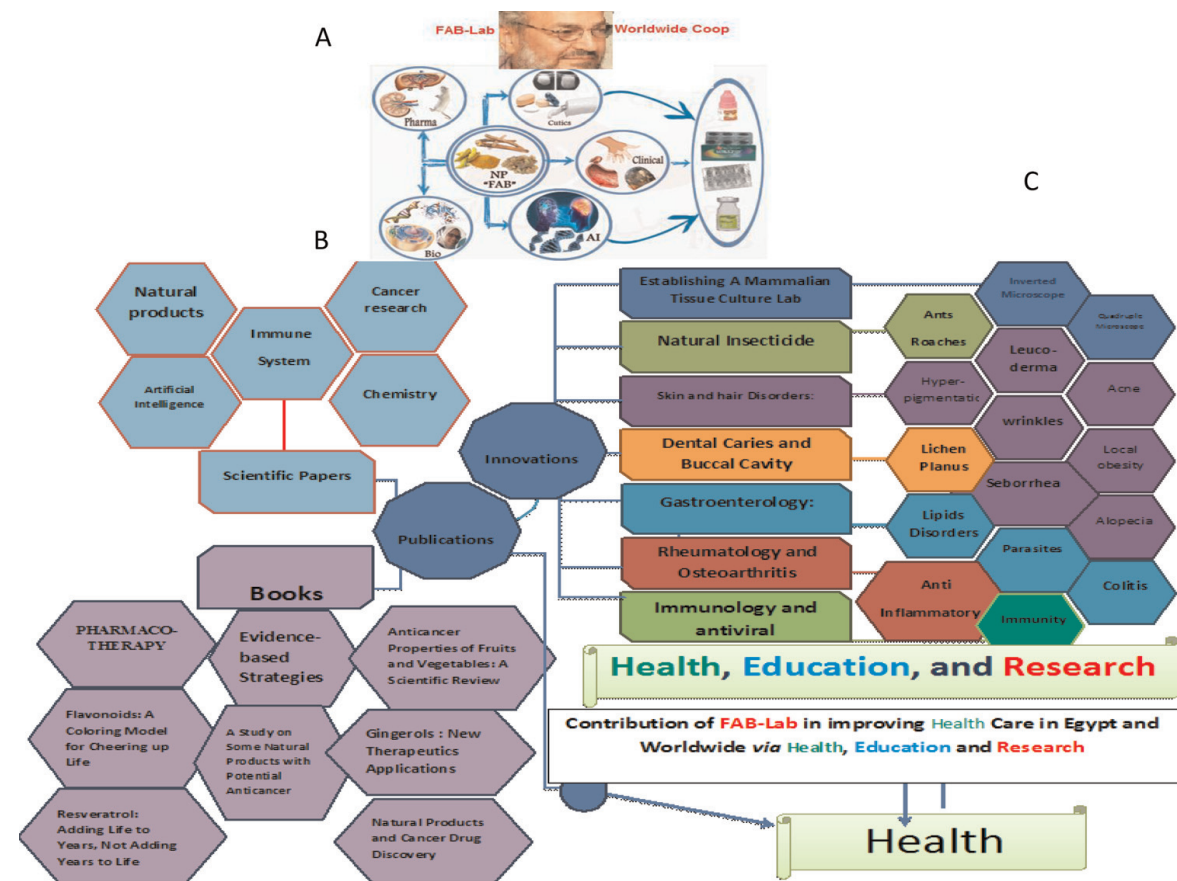


Figure 1.
FAB-lab multidisciplinary team. (A) Research was initiated in the Faculty of Pharmacy and then extended to worldwide cooperation. FAB-lab contributions in improving health care, education, and research collaboration were presented in research and books publications (B), and patents (C).

waste containing phenolic compounds as potential therapeutic agents in many health disorders; e.g., cancer, cataract, degenerative diseases, hyperpigmentation, hyperglycemia, skin disorders, and others, besides contribution in synthesis of nano-silver, green chemistry, click chemistry, and chelating agents for iron overload.

Structures and biological diversity of phenolic compounds isolated in Fab-Lab included but not limited to simple phenolics, e.g., gallic acid, methyl gallate, vaniline, and eugenol and polyphenolic compounds; e.g., flavonoids, curcuminoids, anthraquinones, gingerols, epigallocatechins.

Therefore, this chapter will present some FAB-Lab's success and accomplishments in industrial and environment-friendly chemistry (e.g., green and click chemistry), modulation of enzymes in different biological systems (e.g., tyrosinase, alpha-amylase, hyaluronase, aldose reductase, topoisomerase, and leukotriene hydrolase "LTH4ase," and therapeutic applications (e.g., hepatology, ophthalmology, nephrology, dermatology, dentistry, virology, and metabolic disorders).

3. Industrial and environment-friendly chemistry

3.1 Green chemistry and preparation of silver nanoparticles using natural phenolic compounds

Silver nanoparticles (AgNPs) exhibit unique chemical and biological properties and thus gained extensive interest in commercial applications including food, textiles,

pharmaceuticals, and medical products. Green synthesis is a reliable and eco-friendly process for synthesis of AgNPs, which was reported by FAB-Lab team [24] based on the reducing power of different plant extracts. Forty-two aqueous plant extracts were investigated for their ability to produce AgNPs from aqueous solution of AgNO_3 . Our study showed that the extracts of *Emblica officinalis* fruit, *Psidium guajava* leaves, and *Lawsonia inermis* leaves were able not only to produce AgNPs but also to stabilize the produced nanoparticle. Phytochemical study showed that these extracts contain tannins, polyphenolics, flavonoids, and naphthoquinones, which are responsible for the bioreduction of silver ions to AgNPs (As shown in **Figure 2**). The transmission electron microscopy (TEM) images revealed that the produced AgNPs are characterized by having a spherical and well-dispersed particles with size range from 5 to 30 nm. Interestingly, the AgNPs prepared by *E. officinalis* fruit, *P. guajava* leaves showed nearly the same cytotoxic activity effect as their plant extract. However, AgNPs capped with *L. inermis* exhibited cytotoxic effect against both colon and breast cancer cell lines. This study suggests that AgNPs synthesized and stabilized with *L. inermis* leaves extract could contribute to the development of an appropriate anticancer medication [24].

3.2 Click chemistry and preparation of potential therapeutic agents using natural phenolic compounds

Search for new compounds, e.g., commonly available phenolic compounds, which can be used by using small molecules (units) to join together as building block with heteroatom links.

A click reactions advantage may include high yield products, and less or no by-products, simple reaction conditions, simple available starting materials, simple reagents, and environment-friendly solvents (mainly water), which will help in easy and clean isolation, purification, and crystallization. Therefore, click reactions may

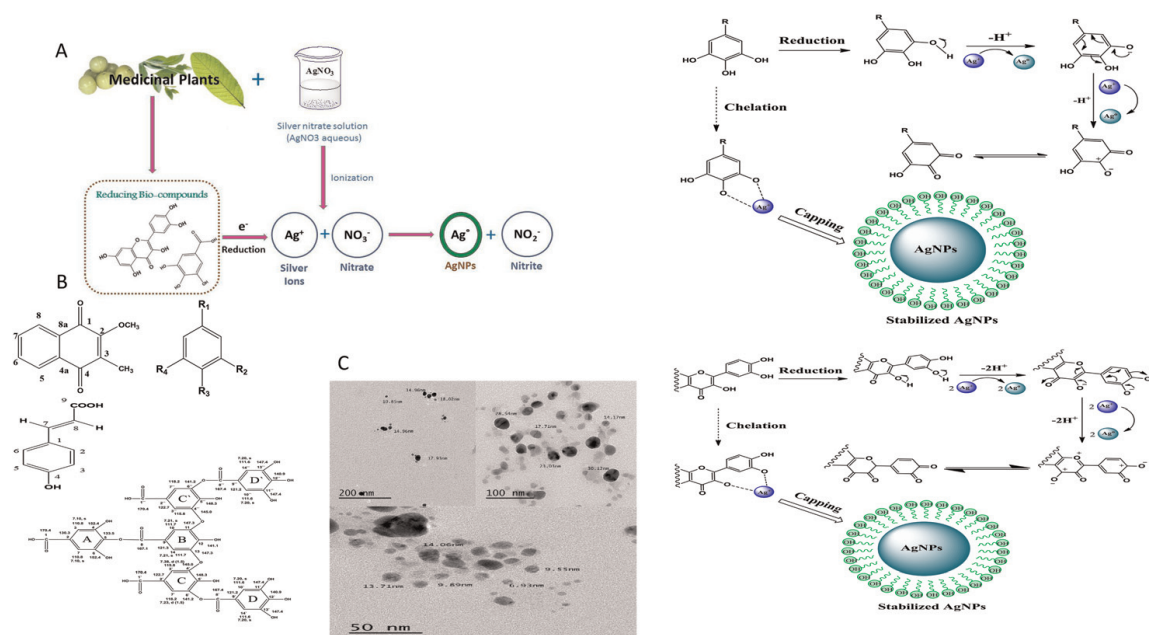


Figure 2.

Preparation of nano-silver particle using natural phenolic compounds; flavonoids (A), naphthoquinone, gallic acid, and hexagalloyl derivatives (B) via chelation, capping, and stabilized silver ion (C).

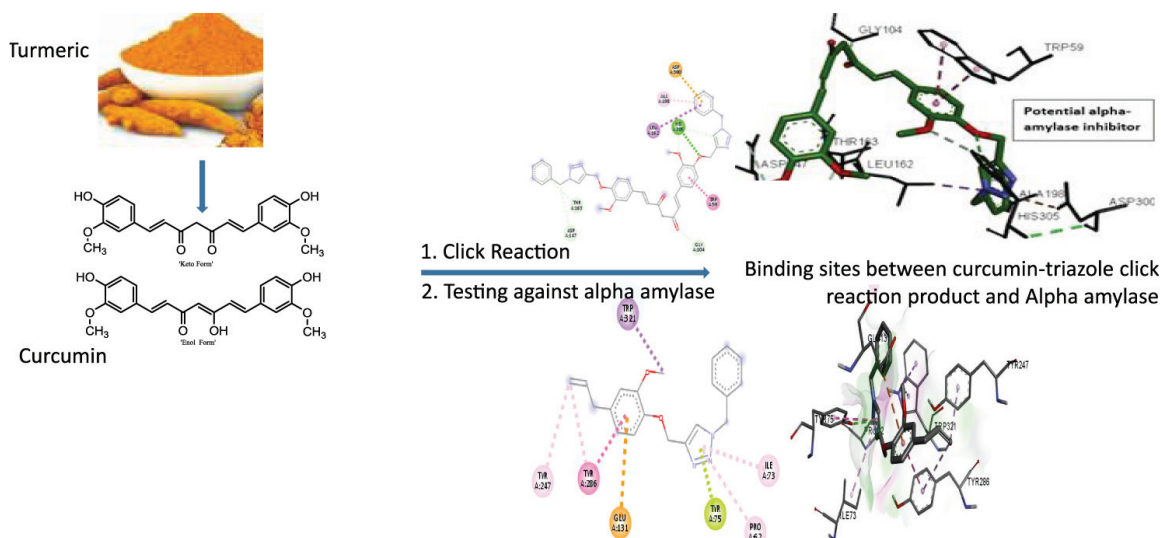


Figure 3.
Curcumin-triazole click reaction product and binding sites between curcumin-triazole click reaction product and alpha amylase.

offer a good alternative to conventional reactions. This prompted us to use vaniline, eugenol, and curcumin in azide-alkyne cycloaddition (AAC) as a major reaction of click chemistry based on the CuAAC [25].

Curcumin was used as a starting material to prepare three new triazole derivatives via 1,3-dipolar cycloaddition (CuAAC) click reaction to produce three triazole derivatives, which were tested against alpha-amylase, which is an essential metabolic enzyme for carbohydrate metabolism. Curcumin-benzyl triazole derivatives showed effective inhibitory activity against alpha-amylase (83.9% inhibition at concentration 1 mg/ml). In silico studies were also performed to predict the binding affinity of the prepared triazoles toward human α -amylase (PDBID: 1u30) (as presented in Figure 3) [25].

3.3 Augmentation of phenolic compounds in edible seed sprouts

Elicitation and physical stimulation during germination are efficient tools to modulate both chemical and biological contents of many important functional foods and medicinal plants. Elicitors from different origins could be used either alone or with hydroponic sprays during germination and growth or right before harvest. A better knowledge on the effect of certain compounds on biosynthetic pathways in responding to specific treatments with elicitors would be a very useful way to augment the production of secondary metabolites or produce new metabolites. This will help in production of high-quality, healthy, and useful medicinal plants and foods. *Moringa oleifera* (MO) leaves extract contains a several active constituents; alkaloids, carotenoids, glucosinolates, polyphenols, tannins, and saponins and is considered as a good biotic elicitor. It was used in this study to enhance both phenolic and antioxidant contents in germinated alfalfa sprouts. Germination of alfalfa seeds in continuous light and soaking seeds in 0.0625, 0.03125 g/L MO extract before germination significantly increases the levels of total phenolics and their antioxidant activity. The maximum amount of flavonoids was exudated after 8 hours of germination. The optimal concentration to elicit maximum phenolic levels was further used to study the biological activities [26].

3.3.1 Histochemical localization of polyphenolic compounds

Localization of phenolic compounds in the different organs and tissues of cotton (*Gossypium barbadense* L. var. Giza 86) plant (seeds, stems, leaves, and roots) was conducted in FAB-Lab. The study revealed the presence of polyphenolic compounds as tiny particles in the cytoplasm of some parenchymatous cells surrounding the lysigenous glands. The obtained data shed more light on our previous results on the antimitotic activity of polyphenolic aldehyde gossypol and why does not affect the growing tip of the plant [27].

4. Developing new therapeutic agents via modulation of biological systems using phenolic compounds

Over 15 years, FAB-Lab team had developed several models for designing new therapeutic agents from phenolic compounds through inhibiting different target enzymes.

4.1 Tyrosinase

Flavonoids contain an alpha-keto group as new type of tyrosinase inhibitors from natural products as potential treatments for hyperpigmentation [28].

4.2 Hyalourindase

The extract of different organs of *Ravenala madagascariensis* (Sonn.) plant showed a good inhibitory activity against hyaluronidase enzyme. Both metabolic analysis and phytochemical studies disclosed the presence of 19 different phenolic compounds, which may present flavone, flavonol, and flavanol glycosides, and aglycone. Specifically, isorhamnetin-7-O-rutinoside, rutin, epiafzelechin, kaempferol, isorhamnetin 7-O-glucoside, and narcissin were isolated and characterized from the butanolic extract of leaves. In docking experiments, narcissin, quercetin 3-O-glucoside, and rutin may interact with enzymes via H-bonding with the Asp111, Gln271, and/or Glu113 residues. These interesting results could be used in pharmaceutical industry to develop new therapeutic agent(s) for skin wrinkles and other cosmetic purposes [29].

4.3 Aldose reductase

The olive and ginkgo leaves extracts with high phenolic contents was proved in an *in vitro* and *ex vivo* inhibitory activity against aldose reductase and could be used as promising therapy for cataract [30, 31].

4.4 Leukotriene hydrolyase

Leukotriene hydrolyase LT4: Synthesis, docking, cytotoxicity, and LTA4H inhibitory activity of phenolic gingerol derivatives as potential colorectal cancer therapy [32, 33].

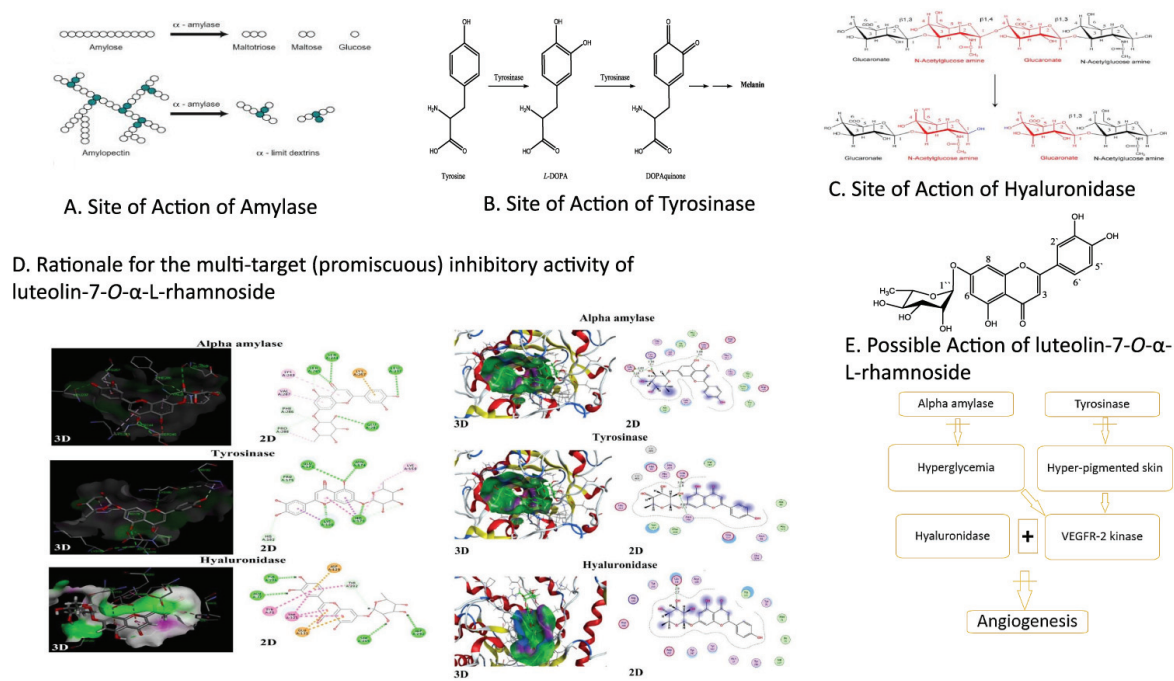


Figure 4.
Developing luteolin-7-O- α -L-rhamnoside as a promiscuous multitarget enzyme inhibitors at three different sites of amylase (A), tyrosinase (B), and hyaluronidase (C). Rationale for the multitarget (promiscuous) inhibitory activity of luteolin-7-O- α -L-rhamnoside (D) and possible action of luteolin-7-O- α -L-rhamnoside (E).

4.5 Promiscuous multitarget inhibitors for treatment of chronic and complicated health disorders

Phenolic compounds proved to be safe and effective multitarget enzyme inhibitors. Screening of over 50 medicinal plant extracts revealed that the phenolic contents of *Punica granatum*, *Phyllanthus emblica*, and *P. guajava* showed good inhibitory activity on α -amylase tyrosinase and hyaluronidase enzymes (as shown in **Figure 4**). These raw data encouraged us in FAB-Lab to go further to develop and design a multitarget drug from phenolic compounds [34–36].

5. Designing a promiscuous multitarget inhibitor against three metabolic enzymes (alpha amylase, tyrosinase, and hyaluronidase)

In principle, we hypothesized the following:

- Alpha amylase inhibitor could inhibit vascular endothelial growth factor receptor 2 (VEGFR-2) through inhibition of high glucose-induced [37]
- Tyrosinase inhibitor could inhibit melanin synthesis and halt the expression of vascular endothelial growth factor (VEGF) [38]
- Hyaluronidase inhibitor could reduce or stop hyaluronic acid fragmentation and subsequently halt the proliferation and endothelial cell migration and capillary formation [39].

Based upon this hypothesis, we have developed in FAB-Lab luteolin-7-O- α -L-rhamnoside, which could be used as a potential multitarget enzyme inhibitor (promiscuous inhibitor) for alpha amylase, tyrosinase, and hyaluronidase.

Luteolin-7-O- α -L-rhamnoside could be used as a potential multitarget enzyme inhibitor in another words, promiscuous enzyme inhibitor, for the possible treatment of various health disorders such as angiogenesis-related disorders.

Luteolin aglycone, when compared with its glycoside, can easily access the catalytic site through 3' and 4'-hydroxy group in ring B (bonded to Cys83) and the 7-hydroxy in ring A (bonded to Gly245, Ala246, and Val248). These data are in agreement with other reports in which luteolin was proven to be a noncompetitive tyrosinase inhibitor.

While luteolin glycoside(5-O- β -D-glucopyranoside) could also be interacted close to Cu and HOO ions as kojic acid and L-tyrosine, luteolin aglycone and luteolin glycoside (7-O- β -D-glucopyranoside) could not. These findings support that sugar moiety at 7 position may have a role in the type of inhibition (i.e., noncompetitive).

Luteolin as a free aglycone has a very weak inhibitory activity toward hyaluronidase in comparison with luteolin-7-O- α -L-rhamnoside. This may refer to the importance of the hydroxyl groups in the rhamnose moiety at 7 position, and this was confirmed by the molecular docking simulation. Because there are two hydroxyl groups that bind to the amino acid residues Asp292 and Ser245 via hydrogen bond interactions.

There were not any reports about luteolin-7-O-rhamnoside inhibitory activity toward the three metabolic enzymes of interest.

In conclusion, more than 50 extracts of different medicinal plants were screened for their biological activities as inhibitors for some metabolism-related enzymes. Extracts with the highest activities were fractionated, and four compounds were isolated, which were found to be multitarget inhibitors for alpha amylase, tyrosinase, and hyaluronidase or at least two of them. Virtual screening and mechanism of action determination studies were performed also for these compounds.

6. Pharmaceutical and therapeutic applications

6.1 Liver research (liver fibrosis, liver cancer, interferon inducer)

Establishing *in vitro*, *in vivo*, and preclinical models for liver fibrosis, liver injury, schistosomiasis, iron-overloaded, fatty liver, and immunosuppression, FAB-Lab team showed that naringin (a flavanol isolated in FAB-Lab grape fruit) exhibited a potent hepatoprotective activity [40]. Recently, it was further prepared in a nanoscopic nanomicelle formula to improve its efficacy and bioavailability as antiulcer and anti-cancer [41]. The prepared formula showed a very good activity in protection of gastric mucosa and suppressed the release cytokines *in vivo* model using ethanol-induced ulcer in rats. Moreover, in *in vitro* cytotoxicity assay using cell lines and EAC-bearing mice, naringin nanomicelle showed an excellent result as cytotoxic and tumor agent. This may prompt us to propose naringin nanomicelles as a nanodrug with prolonged release and enhanced antiulcer as well as antitumor activities [41].

6.2 Colorectal cancer, human breast carcinoma, triple breast cancer

Even though many flavonoids proved their efficacy in different models/assays against colorectal cancer, no solid evidence was about the relation between SAR

(Structure-Activity-Relationship) and colorectal cancer. This prompted the FAB-Lab team to examine the SAR of flavonoids and *in vitro* anticolon cancer using human colon cancer cell line (Caco-2). Surprisingly, the obtained results showed that the OH of C-5 and C-7 in A ring increasingly improved the anticancer effect of flavonoids when compared with 5-FU. In contrary, the presence of glucose moiety or OH— groups in B ring drastically reduced the anticancer activity. In conclusion, FAB-Lab team proposed a novel, hypothesis SAR of flavonoid-colorectal cancer therapy, which may provide a new horizon to better improve management of colorectal cancer [42].

6.3 Antimitotic activity

Several natural phenolic anthraquinone compounds were isolated from different plants and agriculture wastes in FAB-Lab. The salient features and the different biological activity of various anthraquinones compounds depend mainly on the distribution of OH groups in the basic skeleton. The study in FAB-Lab revealed that the presence of OH-group at O-position is a very important feature to portray a potent antimitotic activity (Badria assay) as seen in alizarin, which is the only OH-quinone having an OH— group in an ortho-position. The SAR study revealed that other compounds were active but in the following orders: emodin > aloe emodin > rhein > quinizarin. Interestingly, our results showed that 1-hydroxyanthraquinone could be a carcinogen [43].

Gingerol, a natural phenolic compound, and its derivatives exhibited a broad spectrum against different cancer cell lines and could be also used as a chemosensitizer with currently used anticancer drugs [44].

Ricinine, a simple alkaloid isolated from castor seeds in FAB-Lab, was used to prepare 16 derivatives and tested against SAS-oral cancer cell line in MTT assay versus 5-FU as possible agents for treatment of oral cancer. Sixteen new analogues were synthesized from ricinine. In contrary to 5-FU, the ricinine derivatives were able to suppress the growth of cancer cells at 25 mM [45].

6.4 Cataract

Phenolic compounds from both ginkgo (GK) and olive leaves (OL) extracts were examined both in *in vitro* and *ex vivo* assays against aldose reductase to find potential and selective inhibitors for the enzyme and possible use as a preventive or treatment for cataract. The promising results prompted FAB-Lab team to reveal the possible inhibitory mechanism of GK and OL by using computer-assisted programs. The results revealed that the phenolic compounds could inhibit the polyols pathways via halting the advanced glycation, which may have a crucial role in pathogenesis of cataract [46].

6.5 Idiopathic nephrotic syndrome

Phenolic contents of lyophilized *Citrus paradise* (grape fruit) were prepared in standardized soft gelatin capsules (GF) in FAB-Lab. The prepared capsules (GF) were coadministered with cyclosporine (CsA) for patients diagnosed with idiopathic nephrotic syndrome in Nephrology and Urology center at Mansoura University, Egypt. The coadministration of GF capsules resulted in increased CsA exposure in the range of 10–25%. Moreover, this clinical study proved that CsA-GF coadministration

was found to be safe and well-tolerated as confirmed from laboratory and clinical studies [47].

6.6 Iron chelation (curcumin, mangiferin, catechins)

Catechins (from green tea leaves), curcumin (from turmeric rhizomes), and mangiferin (from mango leaves) were among many other phenolic compounds that had been isolated in FAB-Lab [48, 49]. Iron-overload disorder (hemochromatosis) is one of the major reasons of morbidity. Most of the commonly available iron-chelating agents suffer from many side effects, which pronounced the need for a safe and effective natural iron-chelating agent(s) alternative. Therefore, FAB-Lab team conducted several *in vitro* and *in vivo* studies on selected polyphenol compounds (catechin, curcumin, and mangiferin), which may serve excellent natural alternative for commonly synthetic iron-chelating agents. Different iron-overloaded experimental models were conducted and disclosed the high efficacy of catechin, mangiferin, and curcumin (as shown in **Figure 5**). Subsequently, three very promising alternatives could be used in both clinical and industrial iron-overload or oxidative stress health and/or environmental problems [49].

6.7 Antiviral activity

Several formulae using proniosomes technique were proposed in FAB-Lab to prepare nanocurcumin (NC) as possible antiviral antiherpes (*Herpes simplex* type I) agent in comparison to a commonly used acyclovir (ACV). The results showed that NC exhibited a better and safe activity over ACV against Herpes-simplex Type I. Interestingly, NC-ACV combination reduced the toxicity and enhanced the efficacy that led to 100% plaque reduction over ACV alone [50].

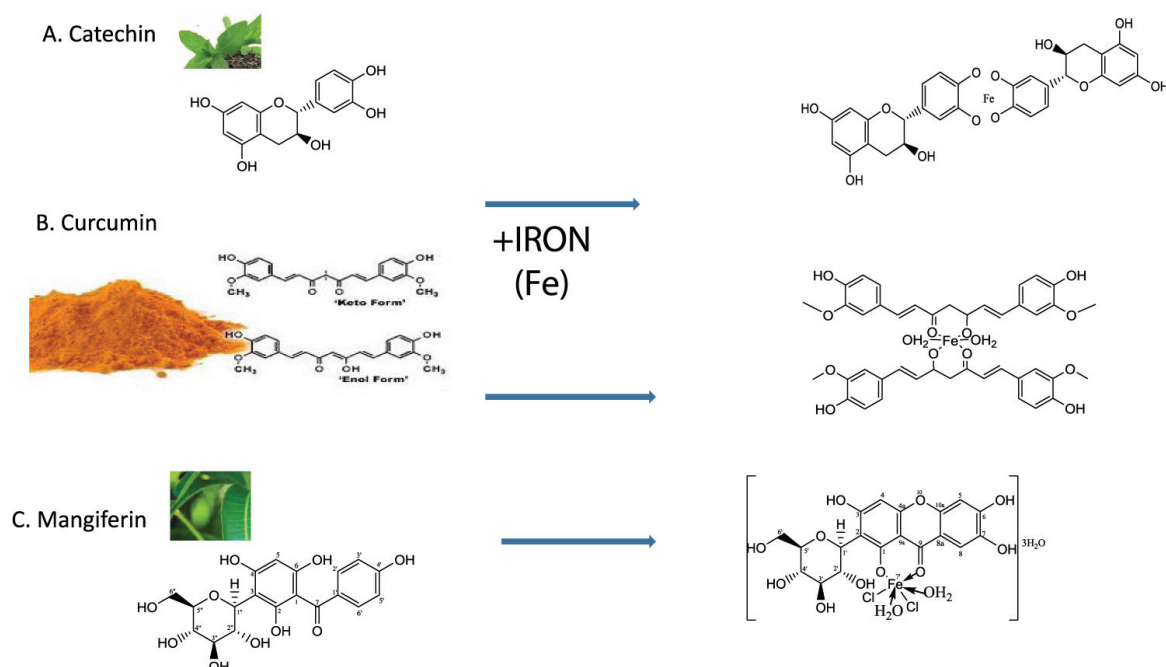


Figure 5. Chelation of iron by catechin from green tea leaves (A), curcumin from turmeric rhizomes (B), and mangiferin from mango leaves (C).

7. Conclusions and future perspective

Phenolic compounds of natural sources, herbs, foods, marine organisms, insects, and other natural sources, still maintain a crucial role in our daily health life in prevention and/or treatment. Therefore, a better utilization of extracts rich in phenolic compounds and/or isolated pure phenolic compounds, e.g., alkaloids, flavonoids, stilbenes, tannins, curcuminoids, coumarins, lignans, quinones, may help in providing the community with chemopreventive properties (e.g., antioxidant, anticarcinogenic, or antimutagenic and antiinflammatory effects). Moreover, phenolic compounds may also contribute in inducing apoptosis by arresting cell cycle, regulating carcinogen metabolism and ontogenesis expression, inhibiting DNA binding and cell adhesion, migration, proliferation, or differentiation, and blocking signaling pathways.

This chapter covers the foremost recent preclinical and clinical research from FAB-Lab and summarizes structural categories and molecular mechanisms of phenolic compounds from medicinal herbs and dietary plants.

Accordingly, the founding factors of FAB-Lab vision were to:

- Protect the environment against all hazards.
- Treat the current diseases using the abundantly available phenolic compounds, whereas many people are suffering worldwide and inspiring from totally indigenous raw materials.
- Conduct basic and simple technology to produce a 100% natural medicine.
- Upon such vision, all research projects, scientific creations, trouble-shooting and problem-solving techniques were based so that the environment was the arena and the main assistant so long as we cared for it and lived in it and with it in harmony. In our turn, FAB-lab team proved the usefulness of phenolic compounds in different aspects by which we can fight contagious and cancerous diseases with hope to add life to our years rather than adding years to life and present a healthy model for cheering up life especially during the turmoil of COVID-19 pandemic [51–55].

Acknowledgements

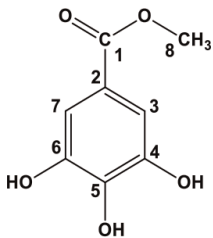
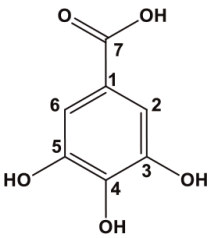
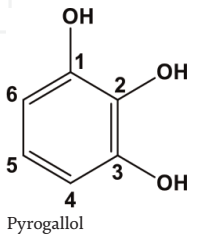
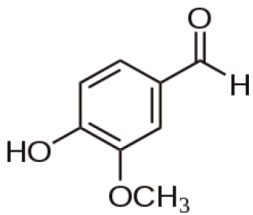
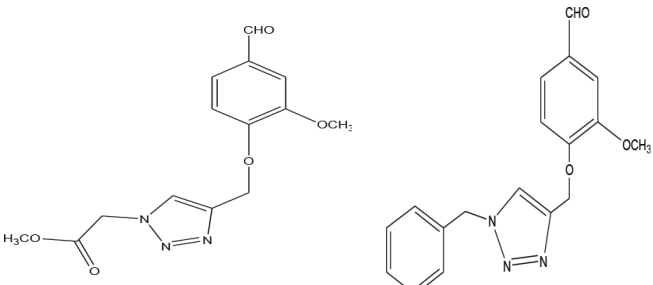
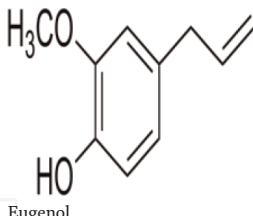
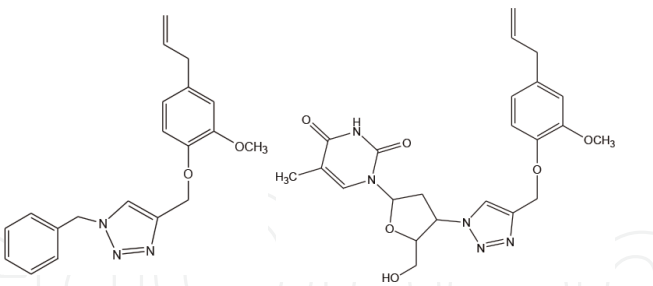
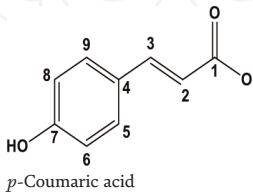
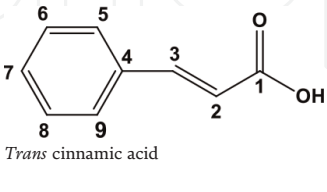
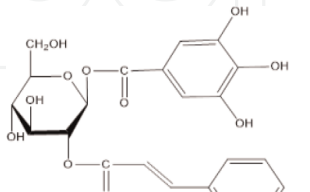
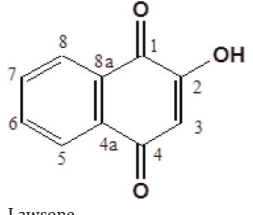
The author acknowledges the support of Academy of Scientific Research and Technology ASRT, the Arab Development Fund, Kuwait, ICRO-UNESCO International, UNESCO Biotechnology, TWAS-ARO, CEC for both research and capacity building grants to FAB-Lab. Also, the author is deeply indebted to the unwavering support and sincere appreciation of Prof. Dr. W.T. Shier (University of Minnesota, USA), Prof. Dr. I. Khan, Prof. Dr. Charles Hufford, and Prof. Dr. M. El-Sohaly (University of Mississippi, USA), Prof. Dr. Francesca Pataculi (College of Medicine, University of Rome), Prof. A. Kumar (Assam University, India), Prof. Dr. Bharat B. Aggarwal (The University of Texas MD Anderson Cancer Center, Houston, Texas), Prof. Dr. Werner E. Müller (Universität Mainz, Germany), Prof. Dirk Selmar (Institut für Pflanzenbiologie, Technische Universität Braunschweig, Germany), Prof. Dr. Amarullah H. Siregar ((Indonesian Community on Functional Advancement Medicine, Jakarta, Indonesia), Prof. Dr. Ibraheim Jantan (Kuala Lumpur, Malaysia), and Prof. Dr. Delgado (Havana, Cuba).

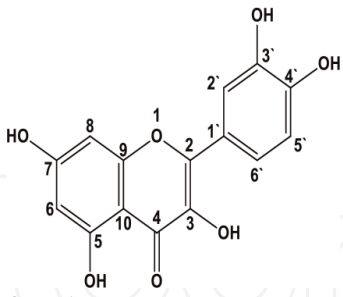
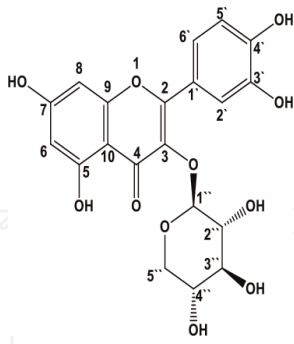
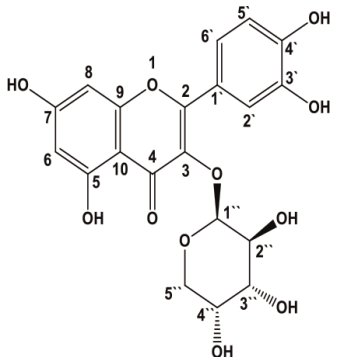
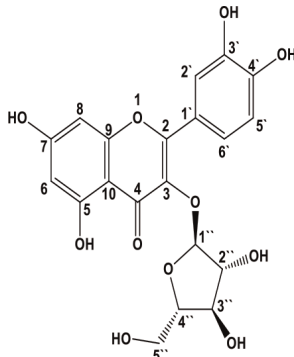
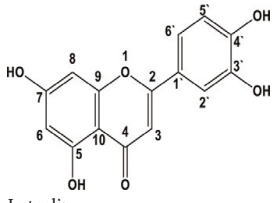
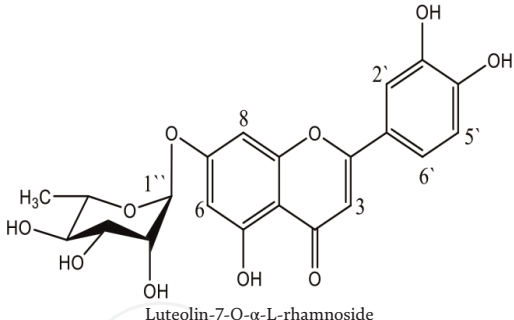
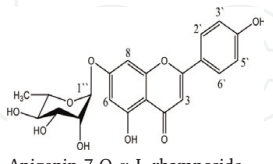
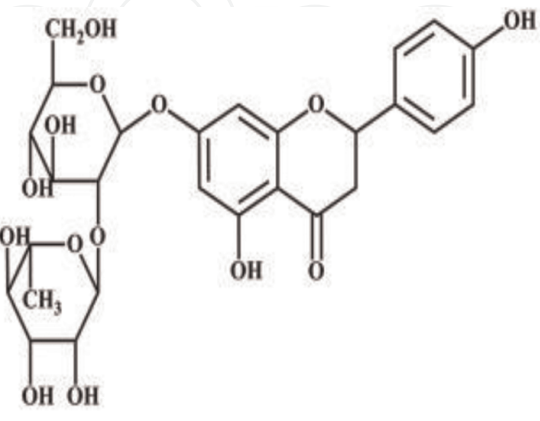
Conflict of interest

The author has declared that no competing or conflict of interests exists.

Appendix

Table 1. Examples of Different Classes of Phenolic Compounds isolated and prepared in FAB-Lab (Liver Research Lab, Mansoura University, Egypt).

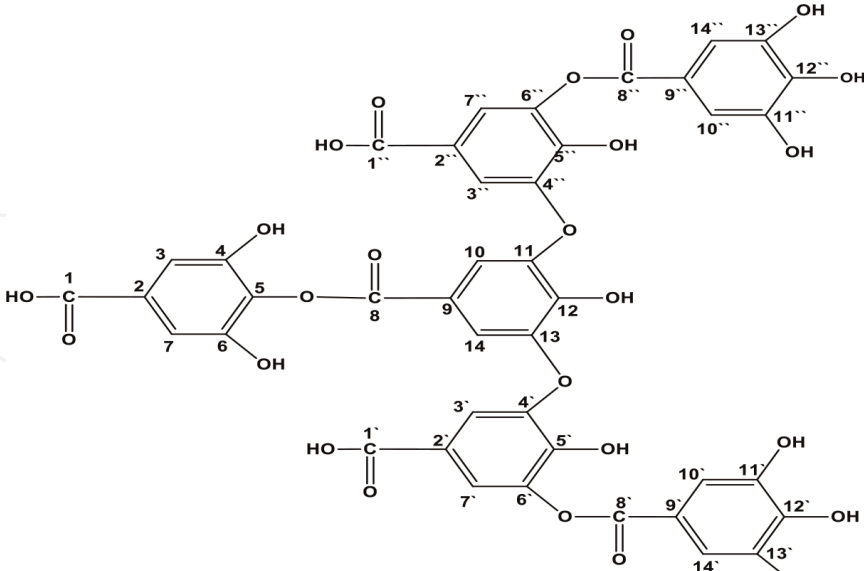
Class	Structure and name		
Simple phenolic compounds	 Methyl gallate	 Gallic acid	 Pyrogallol
	 Vaniline	 Vaniline triazoles (click reaction products)	
	 Eugenol	 Eugenol triazoles (click reaction products)	
	 <i>p</i> -Coumaric acid	 <i>Trans</i> cinnamic acid	 2- <i>O</i> -Cinnamoyl-1- <i>O</i> -galloyl-β-D-glucopyranoside
	 Lawsone		

Class	Structure and name
Polyphenolic compounds	
1. Flavonoids	
	 Quercetin  Quercetin-3-O-β-D-xylopyranoside (reynoutrin)
	 Quercetin-3-O-β-arabinopyranoside  Quercetin 3-O-α-L- arabinofuranoside (avicularin)
	 Luteolin  Luteolin-7-O-α-L-rhamnoside
	 Apigenin-7-O-α-L-rhamnoside  Naringin (4', 5, 7-trihydroxy flavanone 7-rhamnoglucoside) Naringin (4',5,7-trihydroxy flavanone 7-rhamnoglucoside)

Class

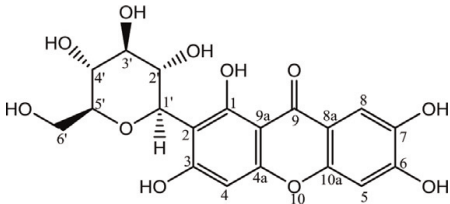
Structure and name

2. Tannins

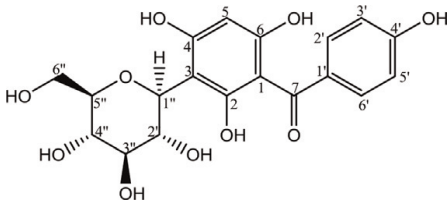


Emblifatmin

1,3,6,7-Tetrahydroxy-9H-xanthen-9-one

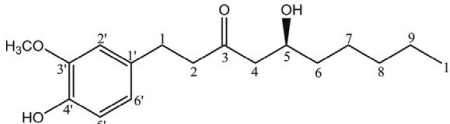


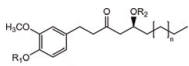
Mangiferin



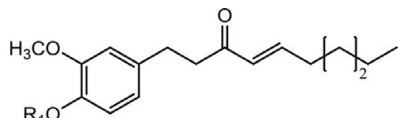
Iriflophenone-3-C-β-D-glucoside

3. Gingerol

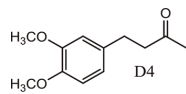




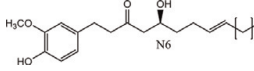
n	R ₁	R ₂
N1	2	H
N2	4	H
N3	6	H
N4	0	H
N5	2	CH ₃
D1	2	Allyl
D3	2	COCH ₃
D5	2	H
D6	2	CH ₃
D10	2	Prenyl



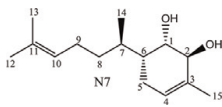
R ₁	
D2	COCH ₃
D7	H
D8	CH ₃
D11	Prenyl



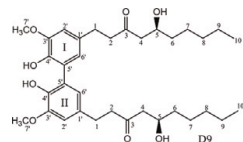
D4



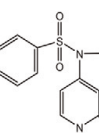
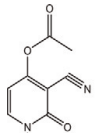
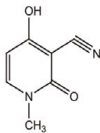
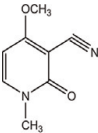
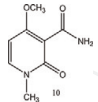
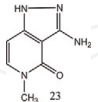
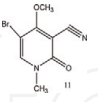
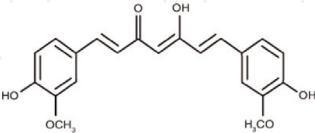
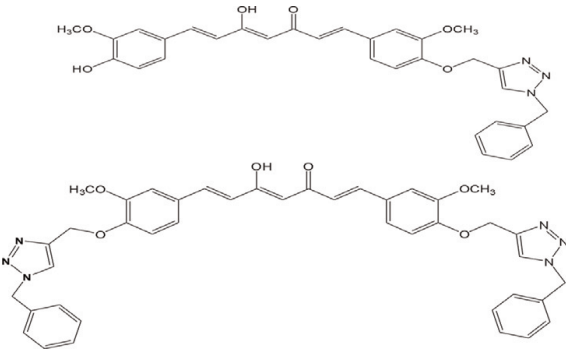
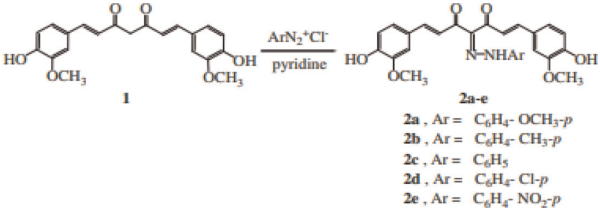
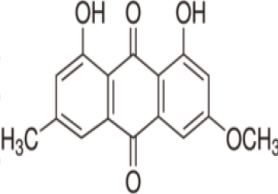
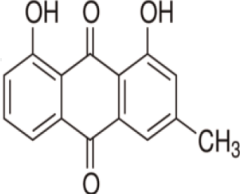
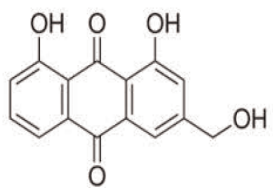
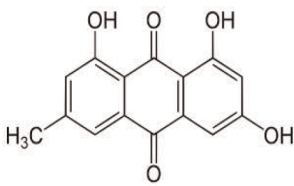
N6



N7



D9

Class	Structure and name
4. Ricinine	 
5. Curcumin	 a. Click Reaction Products (Curcumin-Triazole Derivatives)  b. Preparation of curcumin derivatives  1 2a-e 2a, Ar = C₆H₄-OCH₃-p 2b, Ar = C₆H₄-CH₃-p 2c, Ar = C₆H₅ 2d, Ar = C₆H₄-Cl-p 2e, Ar = C₆H₄-NO₂-p
6. Anthraquinones	 1,8-Dihydroxy-3-methyl anthraquinone (chrysophanol) 1,8-Dihydroxy-3-methyl-6-methoxy anthraquinone (physcion)  1,8-Dihydroxy-3-hydroxy methyl anthraquinone (aloe-emodin)  1,6,8-Trihydroxy-3-methyl anthraquinone (emodin)

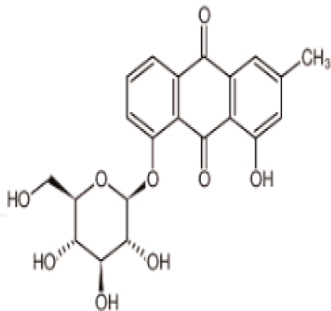
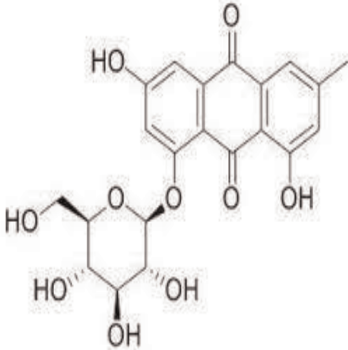
Class	Structure and name
	 Chrysophanol-8-O-β-D-glucopyranoside (chrysophanein)
	 Emodin-8-O-β-D-glucopyranoside

Table 1.
Examples of different classes of phenolic compounds isolated and prepared in FAB-Lab (Liver Research Lab, Mansoura University, Egypt).

Author details

Farid A. Badria
Liver Research Lab, FAB-Lab, Pharmacognosy Department, Faculty of Pharmacy,
Mansoura University, Mansoura, Egypt

*Address all correspondence to: badri002@mans.edu.eg

IntechOpen

© 2022 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 

References

- [1] Badria FA. Is man helpless against cancer? An environmental approach: Antimutagenic agents from Egyptian food and medicinal preparations. *Cancer Letters*. 1994;**84**:1-5
- [2] Badria F, Abou-Mohamed G, El-Mowafy A, Masoud A, Salama O. Mirazid: A new schistosomicidal drug. *Pharmaceutical Biology*. 2001;**39**:127-131
- [3] Lao Y. Clinical study on effect of matriline injection to protect the liver function for patients with primary hepatic carcinoma after trans-artery chemo-embolization (TAE). *Zhong Yao Cai*. 2005;**28**(7):637-638
- [4] Kwon KH, Barve A, Yu S, Huang MT, Kong AN. Cancer chemoprevention by phytochemicals: Potential molecular targets, biomarkers and animal models. *Acta Pharmacologica Sinica*. 2005;**28**(9):1409-1421
- [5] Rudolf E, Andelova H, Cervinka M. Activation of several concurrent proapoptotic pathways by sulforaphane in human colon cancer cells SW620. *Food and Chemical Toxicology*. 2009;**47**(9):2366-2373
- [6] Scheckel KA, Degner SC, Romagnolo DF. Rosmarinic acid antagonizes activator protein-1-dependent activation of cyclooxygenase-2 expression in human cancer and nonmalignant cell lines. *Journal of Nutrition*. 2008;**138**(11):2098-2105
- [7] Sanchez-Fidalgo S, Cardeno A, Villegas I, Talero E, de la Lastra CA. Dietary supplementation of resveratrol attenuates chronic colonic inflammation in mice. *European Journal of Pharmacology*. 2010;**633**(1-3):78-84
- [8] Narisawa T, Fukaura Y, Hasebe M, Ito M, Aizawa R, Murakoshi M, et al. Inhibitory effects of natural carotenoids, alpha-carotene, beta-carotene, lycopene and lutein, on colonic aberrant crypt foci formation in rats. *Cancer Letters*. 1996;**107**(1):137-142
- [9] Sung B, Pandey MK, Ahn KS, et al. Anacardic acid (6-nonadecyl salicylic acid), an inhibitor of histone acetyltransferase, suppresses expression of nuclear factor-kappaB-regulated gene products involved in cell survival, proliferation, invasion, and inflammation through inhibition of the inhibitory subunit of nuclear factor-kappaB alpha kinase, leading to potentiation of apoptosis. *Blood*. 2008;**111**:4880-4891
- [10] Vahid F, Zand H, Nosrat-Mirshekarlou E, et al. The role dietary of bioactive compounds on the regulation of histone acetylases and deacetylases: A review. *Gene*. 2015;**562**:8-15
- [11] Di Paolo M, Papi L, Gori F, Turillazzi E. Natural products in neurodegenerative diseases: A great promise but an ethical challenge. *International Journal of Molecular Sciences*. 2019;**20**(20):5170
- [12] Majtan J, Bucekova M, Jesenak M. Natural products and skin diseases. *Molecules*. 2021;**26**:4489
- [13] Philip N, Leishman S, Walsh L. Potential role for natural products in dental caries control. *Oral Health and Preventive Dentistry*. 2019;**17**(5):479-485
- [14] Alex AF, Spitznas M, Tittel AP, Kurts C, Eter N. Inhibitory effect of epigallocatechin gallate (EGCG), resveratrol, and curcumin on proliferation of human retinal pigment epithelial cells in vitro. *Current Eye Research*. 2010;**35**(11):1021-1033

- [15] Mitra S, Dash R. Natural products for the management and prevention of breast cancer. Evidence-Based Complementary and Alternative Medicine. 2018;**2018**:8324696
- [16] Nagle DG. A perspective on natural products in breast cancer carcinogenesis and chemoprevention. Annals of Carcinogenesis. 2016;**1**(1):1002
- [17] Ko EY, Moon A. Natural products for chemoprevention of breast cancer. Journal of Cancer Prevention. 2015;**20**: 223-231
- [18] Nagle DG, Ferreira D, Zhou YD. Molecules of interest: Epigallocatechin-3-gallate (EGCG): Chemical and biomedical perspectives. Phytochemistry. 2006;**67**:1849-1855
- [19] Cragg GM, Pezzuto JM. Natural products as a vital source for the discovery of cancer chemotherapeutic and chemopreventive agents. Medical Principles and Practice. 2016;**25**: 1-19
- [20] Li Y, Li S, Meng X, Gan R-Y, Zhang J-J, Li H-B. Dietary natural products for prevention and treatment of breast cancer. Nutrients. 2017;**9**(7):728
- [21] Elmali N, Esenkaya I, Harma A, Ertem K, Turkoz Y, Mizrak B. Effect of resveratrol in experimental osteoarthritis in rabbits. Inflammation Research. 2005; **54**:158-162
- [22] Leung CY, Liu L, Wong RNS, Zeng YY, Li M, Zhou H. Saikosaponin-d inhibits T cell activation through the modulation of PKC θ , JNK, and NF- κ B transcriptionfactor. Biochemical and Biophysical Research Communications. 2005;**338**(4):1920-1927
- [23] Ammon HPT. Modulation of the immune system by *Boswellia serrata* extracts and boswellic acids. Phytomedicine. 2010;**17**:862-867
- [24] Badria F, Abouhabieb M, Elbar F. Synthesis of Nanoparticles Using Green Chemistry: Green Synthesis. Germany: Grin Verlag; 2019. ISSN 3346083462. Available from: <https://www.amazon.com/Synthesis-Nanoparticles-Using-Green-Chemistry/dp/3346083462>
- [25] Badria F, Elattar E, Galala A, El-Rady H. Alpha-amylase inhibitory effect and docking studies of some new curcumin-triazole derivatives. Acta Scientific Nutritional Health. 2019;**3**(11):124-129
- [26] Badria F, Abouzeid S. *Moringa oleifera* leaves extract: A potent elicitor for germination of alfalfa sprout with high antioxidant activity. Asian Journal of Research in Pharmaceutical Sciences and Biotechnology. 2019;**7**(4):74-83
- [27] Badria F, Houssen W, Zaghlol M, Halim A. Histochemical localization of polyphenolic compounds in *Gossypium barbadense*. International Journal of Research in Pharmaceutical and Nano Sciences. 2018;**7**(5):200-204
- [28] Badria F, ElGayyar M. A New type of tyrosinase inhibitors from natural products as potential treatments for hyperpigmentation. Bollettino Chimico Farmaceutico. 2001;**140**:267-271
- [29] Mohamed E, Hetta M, Rateb M, Selim M, AboulMagd A, Badria F, et al. Bioassay-guided isolation, metabolic profiling, and docking studies of hyaluronidase inhibitors from *Ravenala madagascariensis*. Molecules. 2020;**25**:1714
- [30] Elimam IA, Liou G, Badria FA. Olive and ginkgo extracts as potential cataract therapy with differential inhibitory activity on aldose reductase. Drug Discoveries and Therapeutics. 2017; **11**(1):41-46

- [31] Muhammad A, Muangchoo K, Muhammad IA, Ajingi Y'u S, Bello AM, Muhammad IY, et al. A molecular modeling study of novel aldose reductase (AR) inhibitors. *AIMS Biophysics*. 2020; 7(4):380-392
- [32] Badria F. New Gingerol Derivative against Human Colorectal Carcinoma Caco-2 Cells (German Edition). Germany: Grin Verlag; 2019. ISSN 3346078817. Available from: <https://www.amazon.com/Gingerol-Derivative-against-Colorectal-Carcinoma/dp/3346078817>
- [33] Low C, Akthar S, Patel D, et al. The development of novel LTA4H modulators to selectively target LTB4 generation. *Scientific Reports*. 2017;7:44449
- [34] Badria F, Ahmed M. Multi target drugs: A new therapeutic approach. *International Journal of Research in Pharmaceutical and Nano Sciences*. 2018;7(5):205-213
- [35] Badria F, Omar R, Galala A, Badria F. Multi-target inhibitory activity of some medicinal plants on alpha-amylase, tyrosinase and hyaluronidase: Potential therapy for treatment diabetes and diabetic complications. *Acta Scientific Nutritional Health*. 2019;3(10):68-75
- [36] Ramsay RR, Popovic-Nikolic MR, Nikolic K, et al. A perspective on multi-target drug discovery and design for complex diseases. *Clinical and Translational Medicine*. 2018;7:3
- [37] Fernando K, Yang H-W, Jiang Y, Jeon Y-J, Ryu B. Diphlorethohydroxycarmalol isolated from *Ishige okamurae* represses high glucose-induced angiogenesis in vitro and in vivo. *Marine Drugs*. 2018;16:375
- [38] Kim M, Shibata T, Kwon S, Park TJ, Kang HY. Ultraviolet-irradiated endothelial cells secrete stem cell factor and induce epidermal pigmentation. *Scientific Reports*. 2018;8:4235
- [39] Park D, Kim Y, Kim H, Kim K, Lee Y-S, Choe J, et al. Hyaluronic acid promotes angiogenesis by inducing RHAMM-TGF β receptor interaction via CD44-PKC δ . *Molecules and Cells*. 2012; 33:563-574
- [40] Badria F, ElKashef H. A potent hepatoprotective agent from group fruit. *Alexandria Journal of Pharmaceutical Sciences*. 1994;8(3):165-169
- [41] Mohamed EA, Abu Hashim II, Yusif RM, Shaaban AAA, El-Sheakh AR, Hamed MF, et al. Polymeric micelles for potentiated antiulcer and anticancer activities of naringin. *International Journal of Nanomedicine*. 2018;13:1009-1027
- [42] Ibrahim A, Sobeh M, Ismail A, Alaa A, Sheashaa H, Sobh M, et al. Free-B-ring flavonoids as potential lead compounds for colon cancer therapy. *Molecular and Clinical Oncology*. 2014 Jul;2(4):581-585
- [43] Badria FA, Ibrahim AS. Evaluation of natural anthracene-derived compounds as antimitotic agents. *Drug Discoveries and Therapeutics*. 2013;7(2):84-89
- [44] Ibrahim AS, Sobh MA, Eid HM, Salem A, Elbelasi HH, El-naggar MH, et al. Gingerol-derivatives: Emerging new therapy against human drug-resistant MCF-7. *Tumor Biology*. 2014; 35(10):9941-9948
- [45] El-Naggar M, Abdel Bar F, Choudhary H, Javadi M, Shimizu K, Kunnumakkara A, et al. Synthesis of new selective cytotoxic ricinine analogues against oral squamous cell carcinoma.

Natural Product Research. 2021 Jul;**35**
(13):2145-2156

Journal of Biomolecular Structure and
Dynamics. 2020:1-6

[46] Badria F, Elgazar A.
Chapter 37—Revealing the molecular
mechanism of *Olea europaea* L. in
treatment of cataract. In: Olives and
Olive Oil in Health and Disease. UK,
USA: Academic Press, Elsevier; 2021.
pp. 445-456

[53] Wu C, Liu Y, Yang Y, Zhang P,
Zhong W, Wang Y, et al. Analysis of
therapeutic targets for SARS-CoV-2
and discovery of potential drugs by
computational methods. Acta
Pharmaceutica Sinica B. 2020;**10**:766-788

[47] Badria FA, Elimam DM, Ibrahim AS,
Hamdy AF, El-Husseini A, et al.
Management of idiopathic nephrotic
syndrome: Co-administration of
cyclosporine and lyophilized grapefruit
juice. Biomed Discoveries: BMDC-102.
2018;**1**(5):104-108. DOI: 10.29011/
BMDC-102.100002

[54] Manoharan Y, Haridas V,
Vasanthakumar KC, Muthu S,
Thavoorullah FF, Shetty P. Curcumin:
A wonder drug as a preventive measure
for COVID19 management. Indian
Journal of Clinical Biochemistry. 2020;
35:373-375

[48] Badria FA, Ibrahim AS, Badria AF,
Elmarakby AA. Curcumin attenuates
iron accumulation and oxidative stress in
the liver and spleen of chronic iron-
overloaded rats. PLoS One. 2015;**10**(17):
e0134156

[55] Williamson G, Kerimi A. Testing of
natural products in clinical trials
targeting the SARS-CoV-2 (Covid-19)
viral spike protein-angiotensin
converting enzyme-2 (ACE2)
interaction. Biochemical Pharmacology.
2020;**178**:114123

[49] Badria FA, Suliman SN, Elsbaey M,
El-Naggar MH. Bio-guided fractionation
and iron chelating activity of agricultural
residues. Drug Discoveries and
Therapeutics. 2018;**12**(5):299-303

[50] Badria FA, Abdelaziz AE,
Hassan AH, Elgazar AA, Mazyed EA.
Development of provesicular
nanodelivery system of curcumin as a
safe and effective antiviral agent:
Statistical optimization, in vitro
characterization, and antiviral
effectiveness. Molecules. 2020;**25**:5668

[51] Paraiso IL, Revel JS, Stevens JF.
Potential use of polyphenols in the battle
against COVID-19. Current Opinion in
Food Science. 2020;**32**:149-155

[52] Hendaus MA. Remdesivir in the
treatment of coronavirus disease 2019
(COVID-19): A simplified summary.