

OPEN ACCESS



Journal of
Medicinal Plants Research

25 March 2019
ISSN 1996-0875
DOI: 10.5897/JMPR
www.academicjournals.org

 **ACADEMIC
JOURNALS**
expand your knowledge

About JMPR

The Journal of Medicinal Plants Research (JMPR) provides researchers, students and academicians an avenue to present their findings on the value of medicinal plants, indigenous medications, ethnobotany and ethnomedicine, herbal medicines and the cultivation of aromatic and medicinal plants.

The journal will consider for publication original research, reviews and meta-reviews, and short communication on areas covering nutraceuticals, drug discovery and development, pharmacopoeia, traditional medicine, monographs, and natural products research.

The Journal of Medicinal Plants Research is indexed in:

[CAB Abstracts](#) [CABI's Global Health Database](#) [Chemical Abstracts \(CAS Source Index\)](#) [China National Knowledge Infrastructure \(CNKI\)](#) [Google Scholar](#) [Matrix of Information for The Analysis of Journals \(MIAR\)](#) [ResearchGate](#)

Open Access Policy

Open Access is a publication model that enables the dissemination of research articles to the global community without restriction through the internet. All articles published under open access can be accessed by anyone with internet connection.

The African Journals of Biotechnology is an Open Access journal. Abstracts and full texts of all articles published in this journal are freely accessible to everyone immediately after publication without any form of restriction.

Article License

All articles published by Journal of Medicinal Plants Research are licensed under the [Creative Commons Attribution 4.0 International License](#). This permits anyone to copy, redistribute, remix, transmit and adapt the work provided the original work and source is appropriately cited. Citation should include the article DOI. The article license is displayed on the abstract page the following statement:

This article is published under the terms of the [Creative Commons Attribution License 4.0](#) Please refer to <https://creativecommons.org/licenses/by/4.0/legalcode> for details about [Creative Commons Attribution License 4.0](#)

Article Copyright

When an article is published by in the Journal of Medicinal Plants Research, the author(s) of the article retain the copyright of article. Author(s) may republish the article as part of a book or other materials.

When reusing a published article, author(s) should;

Cite the original source of the publication when reusing the article. i.e. cite that the article was originally published in the Journal of Medicinal Plants Research. Include the article DOI

Accept that the article remains published by the Journal of Medicinal Plants Research (except in occasion of a retraction of the article)

The article is licensed under the Creative Commons Attribution 4.0 International License.

A copyright statement is stated in the abstract page of each article. The following statement is an example of a copyright statement on an abstract page.

Copyright ©2016 Author(s) retains the copyright of this article.

Self-Archiving Policy

The Journal of Medicinal Plants Research is a RoMEO green journal. This permits authors to archive any version of their article they find most suitable, including the published version on their institutional repository and any other suitable website.

Please see <http://www.sherpa.ac.uk/romeo/search.php?id=213&fIDnum=|&mode=simple&la=en>

Digital Archiving Policy

The Journal of Medicinal Plants Research is committed to the long-term preservation of its content. All articles published by the journal are preserved by [Portico](#). In addition, the journal encourages authors to archive the published version of their articles on their institutional repositories and as well as other appropriate websites..

<https://www.portico.org/publishers/ajournals/>

Metadata Harvesting

The Journal of Medicinal Plants Research encourages metadata harvesting of all its content. The journal fully supports and implements the OAI version 2.0, which comes in a standard XML format. [See](#)

[Harvesting Parameter](#)

Memberships and Standards



Academic Journals strongly supports the Open Access initiative. Abstracts and full texts of all articles published by Academic Journals are freely accessible to everyone immediately after publication.



All articles published by Academic Journals are licensed under the [Creative Commons Attribution 4.0 International License \(CC BY 4.0\)](#). This permits anyone to copy, redistribute, remix, transmit and adapt the work provided the original work and source is appropriately cited.



[Crossref](#) is an association of scholarly publishers that developed Digital Object Identification (DOI) system for the unique identification published materials. Academic Journals is a member of Crossref and uses the DOI system. All articles published by Academic Journals are issued DOI.

[Similarity Check](#) powered by iThenticate is an initiative started by CrossRef to help its members actively engage in efforts to prevent scholarly and professional plagiarism. Academic Journals is a member of Similarity Check.

[CrossRef Cited-by](#) Linking (formerly Forward Linking) is a service that allows you to discover how your publications are being cited and to incorporate that information into your online publication platform. Academic Journals is a member of [CrossRef Cited-by](#).



Academic Journals is a member of the [International Digital Publishing Forum \(IDPF\)](#). The IDPF is the global trade and standards organization dedicated to the development and promotion of electronic publishing and content consumption.



[COUNTER](#) (Counting Online Usage of Networked Electronic Resources) is an international initiative

serving librarians, publishers and intermediaries by setting standards that facilitate the recording and reporting of online usage statistics in a consistent, credible and compatible way. Academic Journals is a member of [COUNTER](#)



[Portico](#) is a digital preservation service provided by ITHAKA, a not-for-profit organization with a mission to help the academic community use digital technologies to preserve the scholarly record and to advance research and teaching in sustainable ways.

Academic Journals is committed to the long-term preservation of its content and uses [Portico](#)



Academic Journals provides an [OAI-PMH](#)(Open Archives Initiatives Protocol for Metadata Harvesting) interface for metadata harvesting.

Contact

Editorial Office: impr@academicjournals.org

Help Desk: helpdesk@academicjournals.org

Website: <http://www.academicjournals.org/journal/JMPR>

Submit manuscript online <http://ms.academicjournals.org>

Academic Journals
73023 Victoria Island, Lagos, Nigeria
ICEA Building, 17th Floor, Kenyatta Avenue, Nairobi, Kenya

Editor-in-chief

Prof. Akah Peter Achunike
Department of Pharmacology & Toxicology
University of Nigeria
Nsukka,

Nigeria.

Associate Editors

Dr. Luís Cláudio Nascimento da Silva

Post-graduation program of Microbial Biology.
CEUMA University
Rua Josué Montello, nº 1, Renascença II
São Luís - MA, CEP 65.075-120

Dr. Isiaka A. Ogunwande

Department of Chemistry
Lagos State University
Ojo,
Nigeria.

Dr. Bachir Raho Ghalem

Biology Department
University of Mascara
Algeria.

Dr. Pramod V Pattar

Department of Botany
Davangere University
Karnataka,
India.

Dr. Parichat Phumkhachorn

Department of Biological Science,
Faculty of Science,
Ubon Ratchathani University,
Ubon Ratchathani 34190,
Thailand.

Dr. Anthony Swamy

Department of Chemistry
School of Science and Technology
University of Eastern Africa
Baraton,
Kenya.

Dr. Arvind K Tomer

Department of Chemistry
University of Phagwara
Punjab
India

Dr. Foluso Oluwagbemiga Osunsanmi

Department of Agricultural Science,
University of Zululand,
South Africa.

Associate Editors

Dr. Shikha Thakur

Department of Microbiology,
Sai Institute of Paramedical and Allied Sciences,
India.

Dr. Naira Pelógia

Institute of Basic Sciences,
Taubaté University,
Brazil

Dr. Ravichandran Veerasamy

Faculty of Pharmacy
AIMST University
Semeling,
Malaysia.

Dr. Bellamkonda Ramesh

Department of Food Technology,
Vikrama Simhapuri University,
India

Table of Content

Bio-guided identification of antiglycative constituents from the leaves of *Mangifera indica* L.

129

Samba Fama Ndoye, Didier Fraisse, Blandine Akendengué, Rokhaya Sylla Gueye, Cheikh Sall, Mael Gainche, Insa Seck, Catherine Felgines, Matar Seck and François Senejoux

Full Length Research Paper

Bio-guided identification of antiglycative constituents from the leaves of *Mangifera indica* L.

Samba Fama Ndoye¹, Didier Fraisse², Blandine Akendengué³, Rokhaya Sylla Gueye¹, Cheikh Sall⁴, Mael Gainche⁵, Insa Seck¹, Catherine Felgines², Matar Seck¹ and François Senejoux^{2*}

¹Laboratory of Organic and Therapeutic Chemistry, Faculty of Medicine, Pharmacy and Odontology, Cheikh Anta Diop University, PB 5005 Dakar-Fann, Sénégal.

²Université Clermont Auvergne, INRA, UNH, F-63000 Clermont-Ferrand, France.

³Department of Pharmacology and Toxicology, Faculty of Medicine and Health Sciences (USS). PB 4009 Libreville, Gabon.

⁴Laboratory of Chemistry, Training and Research Unit of Health, Thiès University, PB 967 Thiès, Sénégal.

⁵Université Clermont Auvergne, CNRS, SIGMA Clermont, ICCF, F-63000 Clermont-Ferrand, France.

Received 10 January, 2019; Accepted 18 February, 2019

Advanced glycation end-products (AGEs) have been shown to be implicated in many degenerative disorders as well as diabetic pathology. Of interest, several natural compounds including phenolic constituents are capable of inhibiting the formation of AGEs. Bio-guided fractionation of a methanol extract from *Mangifera indica* leaves led to the characterization of six antiglycative constituents including gallic acid (1), iriflophenone-3-C- β -D-glucoside (2), mangiferin (3), iriflophenone-3-C-(2'-O-galloyl)- β -D-glucoside (4), hyperoside (5) and isoquercitrin (6). With IC₅₀ values lower than that of aminoguanidine, the six identified phenolic compounds can be regarded as remarkable inhibitors of advanced glycation end products formation and *M. indica* leaves should be considered as a potential nutraceutical resource to prevent carbonyl stress-related diseases.

Key words: *Mangifera indica*, antiglycation, radical scavenging, phenolics, benzophenone.

INTRODUCTION

Mangifera indica L. (family: Anacardiaceae) is widely growing in many parts of the world particularly in tropical countries (Rodeiro et al., 2006). In traditional medicine, leaves of *M. indica* are employed to treat a wide range of diseases including malaria, diabetes, diarrhea, dysentery and so on (Yakubu et al., 2015). It has been reported that its bioactive compounds are ascorbic acid, carotenoids as well as phenolic derivatives including gallotannins, flavonoids, xanthenes and benzophenones (Shaheen et

al., 2017). These constituents have been shown to exert several interesting pharmacological activities such as antimicrobial, anti-inflammatory, immunomodulatory, analgesic and antidiabetic effects (Fernández-Ponce et al., 2015; Vasil'ev et al., 2006).

Of interest, all these properties can be, at least in part, related to positive action on oxidative and/or carbonyl stress (Halake et al., 2016; Mildner-Szkudlarz et al., 2017). It has to be noted that the potent antioxidant

*Corresponding author. E-mail: francois.senejoux@uca.fr. Fax: +33 4 73 17 80 37.

activity of mango leaves has already been reported by different studies (Pereira et al., 2007; Fernández-Ponce et al., 2012; Ling et al., 2009). By contrast, very limited investigations have been done regarding inhibitory effects on the formation of advanced glycation end products (AGEs) (Itoh et al., 2017). AGEs are the final products of a nonenzymatic reaction, also known as Maillard reaction, occurring between reducing sugars and nucleic acids, lipids or free amino groups of proteins. Numerous studies have demonstrated that the formation and accumulation of AGEs can accelerate the ageing process (Kim et al., 2017).

Additionally, AGEs are involved in the development of numerous pathologies such as atherosclerosis, neurodegenerative diseases as well as diabetic complications (Yang et al., 2018). Inhibition of the formation of these harmful glycotoxins is thus considered as a promising preventive or therapeutic target for a wide range of disorders (Brings et al., 2017) and increasing consideration is recently being given to the evaluation of phytoconstituents as antiglycating agents.

The present study aimed thus at performing a bio-guided fractionation of a methanolic extract from mango leaves in order to identify potential AGEs inhibition constituents. *In vitro* bovine serum albumin/D-ribose fluorimetric assay was chosen to evaluate the AGEs inhibition properties of the fractions and compounds. Knowing that scavenging reactive oxygen species is also considered as a mechanism of AGEs inhibition (Reddy et al., 2006), antioxidant activity was also assessed by using colorimetric DPPH assay.

MATERIALS AND METHODS

Reagents

Methanol, dichloromethane, ethyl acetate, butanol, trifluoroacetic acid, acetonitrile, D-ribose, bovine serum albumin (BSA), aminoguanidine hydrochloride, gallic acid, 1,1-diphenyl-2-picrylhydrazyl (DPPH), Trolox, fluorescein, 2,2'-azobis(2-methylpropionamide) dihydrochloride, Iron (II) chloride and ferrozine were bought from Sigma-Aldrich (Saint-Quentin Fallavier, France). Ethylenediaminetetraacetic acid disodium salt (EDTA) was purchased from Fisher Chemical (Illkirch, France).

Instrumentation

Proton and carbon nuclear magnetic resonance spectra were recorded in acetone-d₆ on a Bruker DRX 500 spectrometer (¹H:500 MHz, ¹³C:125 MHz) (Bruker Biospin SAS, Wissembourg, France). HPLC analyses were performed with a reverse phase column (Uptisphere[®] C18, 250 mm × 4.6 mm, 3.5 μm particle size) using a UHPLC Ultimate 3000 RSLC apparatus with a DAD UV/VIS 3000 RS detector (Thermo-Fisher Scientific, Germany) and mass spectral analysis was carried out on a Orbitrap Q-Exactive (Thermo-Fisher Scientific, Germany).

Plant material

M. indica leaves (500 g) were collected from cultivated trees at Diender, Senegal, in July 2016 and identified by Dr. William Diatta. A voucher specimen (N°1166 *M. indica* L.) has been deposited in a

laboratory herbarium (Laboratory of Pharmacognosy, Faculty of Medicine, Pharmacy and Odontology from University Cheikh Anta Diop of Dakar, Senegal).

Extraction and isolation of bioactive compounds

The air-dried plant material was powdered and macerated twice for 48 h with methanol at room temperature. The extract was then filtered and methanol was completely removed under reduced pressure on a rotary evaporator.

Crude methanol extract (20 g) was dissolved in distilled water and the aqueous solution was successively partitioned with dichloromethane, ethyl acetate and butanol. Each resulting solvent fraction was concentrated as described earlier to yield a dichloromethane fraction (DF, 1.68 g), an ethyl acetate fraction (EAF, 5.32 g), a butanol fraction (BF, 6.81 g) and an aqueous fraction (AF, 5.93 g). A portion of BF (1.5 g) was fractionated using steric exclusion column chromatography (Sephadex[®] LH-20, 90 g) eluted with a MeOH and water gradient system (60:40 to 80:20), yielding a total of 12 combined fractions. Fraction 5 afforded directly compound 2 (220 mg). Besides, compound 4 was detected as the major constituent of fraction 7 (150 mg). Further purification was performed by mean of semi-preparative HPLC (Nucleosil[®] RP-18, 250 mm × 100 mm, 5 μm particle size) eluted with a mobile phase consisting of water containing 0.1% trifluoroacetic acid and acetonitrile to yield 15 mg of compound 4. Compounds 2 and 4 were unambiguously characterized on the basis of their MS and NMR data as well as through comparison with published reports (Barreto et al., 2008; Pranakhon et al., 2015).

Iriflophenone-3-C-β-D-glucoside (2): ESI-MS *m/z* 407.0980 [M – H][–] (calcd for C₁₉H₁₉O₁₀, 407.0978). ¹H NMR (acetone-d₆) δ: 3.40–3.70 (4H, m), 3.85 (2H, br s), 4.93 (1H, d, *J* = 9.75 Hz), 5.99 (1H, s), 6.85 (2H, d, *J* = 8.75 Hz), 7.64 (2H, d, *J* = 8.75 Hz).

Iriflophenone 3-C-(2'-O-galloyl)-β-D-glucoside (4): ESI-MS *m/z* 559.1091 [M – H][–] (calcd for C₂₆H₂₃O₁₄, 559.1088). ¹H NMR (acetone-d₆) δ: 3.50–3.85 (3H, m), 3.89 (2H, br s), 5.18 (1H, d, *J* = 10 Hz), 5.43 (1H, t, *J* = 10 Hz), 5.89 (1H, s), 6.83 (2H, d, *J* = 7.5 Hz), 7.06 (2H, s), 7.61 (2H, br s).

Evaluation of antiglycation activity

Inhibition of AGEs formation was conducted according to Derbré et al. (2010). Briefly, 40 μL of bovine serum albumin (BSA, 25 mg/mL), 40 μL of D-ribose (120 mM) and 20 μL of sample solutions were incubated at 37°C in a phosphate buffer, 50 mM, pH 7.4. Sample solutions (extract, fractions and pure compounds) were prepared in phosphate buffer (50 mM, pH = 7.4) and DMSO (final concentration 1% (v/v)). Extract and fractions were evaluated at final concentrations of 0.05 to 1 mg/mL while pure compounds were assessed at concentrations of 25 to 500 μM. Aminoguanidine, a widely used inhibitor of AGEs formation (Abdallah et al., 2016; Yang et al., 2018), was employed as positive control (0.5 to 10 mM). Complete reaction mixture including BSA and ribose in PBS was used as negative control (100% of AGEs formation). After 24 h of incubation, AGEs fluorescence was measured with a microplate reader (TECAN infinite F200 PRO) using 370 and 440 nm as the excitation and emission wavelengths, respectively. The IC₅₀ value was calculated from the linear regression analysis of dose-response curve plotting extract or compounds concentration versus inhibition percentage of AGEs formation. All analyses were performed in triplicate and results were expressed as mean ± standard error of mean (SEM).

Evaluation of radical scavenging activity

The DPPH radical scavenging activity was evaluated according to a

Table 1. Antiglycation and DPPH radical scavenging activities of *Mangifera indica* methanol extract and its fractions.

Extract	AGEs inhibition	DPPH scavenging activity
	IC ₅₀ (µg/mL)	(µmol TE/g)
<i>Mangifera indica</i> methanol extract	165 ± 2	2 139 ± 146
Dichloromethane fraction	260 ± 13	1 058 ± 29
Ethyl acetate fraction	149 ± 9	4 705 ± 236
Butanol fraction	116 ± 7	1 884 ± 166
Aqueous fraction	> 400	383 ± 37
Aminoguanidine	259 ± 7	ND

Antiglycation and antioxidant activities are indicated as means ± SEM (n = 3). TE: Trolox equivalent, ND: not determined

previously published method (Meda et al., 2017). Briefly, 10 µL of extract or fractions (0.1-2.5 mg/mL in methanol) or pure compounds (1-40 mM in methanol) were added to 2.5 mL of fresh DPPH solution (25 µg/mL in methanol). After 30 min of incubation, the decrease in DPPH absorbance was recorded at 515 nm. A standard curve of Trolox in the range of 0.1 to 6 mM was constructed ($R^2 = 0.9978$, $y = 1101.1x + 1.5196$) and results were indicated as µmol of Trolox Equivalents per g (µmol TE/g) for fractions and as IC₅₀ for pure compounds. Each assay was conducted in triplicate and results were expressed as mean ± SEM.

RESULTS AND DISCUSSION

M. indica methanolic extract (MIME) was first evaluated for its antiglycation and antioxidant activities. As illustrated in Table 1, results indicated that the studied extract exerted very potent anti-AGEs and radical scavenging effects. Indeed, with an IC₅₀ value of 165 ± 2 µg/mL, MIME was shown to possess a stronger AGEs inhibition activity than the positive control aminoguanidine (259 ± 7 µg/mL). Consistently with previous investigations of *M. indica* leaves (Ling et al., 2009), a substantial DPPH radical scavenging effect was also highlighted (2139 ± 146 µmol Trolox equivalent (TE)/gram of dry extract). The whole extract was thus submitted to liquid-liquid fractionation using solvents of increasing polarities, yielding dichloromethane (DF), ethyl acetate (EAF), butanol (BF) and aqueous (AF) fractions. As indicated in Table 1, BF was shown to exert the highest AGEs inhibition activity as demonstrated by its very low IC₅₀ value of 116 ± 7 µg/mL. By contrast, the best DPPH radical scavenging activity was obtained for EAF, highlighting the fact that the most potent anti-AGEs compounds of *M. indica* leaves were not the best DPPH radical scavengers. Taking these data into consideration, we thus embarked upon an investigation of BF chemical composition, seeking for new anti-AGEs natural compounds.

HPLC-DAD/MS analyses were performed to identify the main constituents of BF. As shown in Figure 1, six major compounds were detected at a wavelength of 280 nm. Compounds 1, 3, 5 and 6 were respectively identified as gallic acid, mangiferin, hyperoside and isoquercitrin by

comparing their retention times, UV spectra and MS data (Table 2) with those of reference commercial standards. Conversely, compounds 2 and 4 did not match with any available standards and purification of these two constituents was achieved to unequivocally determine their structures. A portion of BF was then submitted to steric exclusion column chromatography to afford directly compound 2. This constituent was unambiguously characterized as iriflophenone-3-C-β-D-glucoside on the basis of its MS (Barreto et al., 2008) and NMR data (Pranakhon et al., 2015). Further purification by mean of semi-preparative HPLC led to the isolation of compound 4. Analysis of its ¹H and ¹³C NMR data allowed the characterization of a benzophenone glycoside acylated with a galloyl unit. Deeper investigation of 2D NMR spectra led to the unambiguous identification of iriflophenone 3-C-(2'-O-galloyl)-β-D-glucoside. Of note, spectral data of this very unusual compound were in agreement with a previous chemical study of *M. indica* leaves (Barreto et al., 2008) which constituted the sole description of this constituent in plant kingdom.

As indicated in Table 3, the six identified constituents were all shown to exert substantial inhibitory activity against *in vitro* protein glycation, as attested by their IC₅₀ values lower than that of aminoguanidine. With IC₅₀ values ranging from about 100 µM, compounds 3, 5 and 6 were determined as the most potent inhibitors of the studied fraction. Of note, these results are consistent with previous published studies highlighting the strong anti-AGEs capacity of xanthone derivatives and flavonoid glycosides (Abdallah et al., 2017; Derbré et al., 2010). More precisely, the potent antiglycation activities of compounds 3, 5 and 6 have been previously reported by two distinct studies (Itoh et al., 2017; Kim et al., 2011) using glucose or fructose as reducing sugars. By contrast, data regarding benzophenone constituents are scarcer and the noticeable antiglycation activity of compound 4 is firstly reported. As illustrated in Table 3, compounds 3, 4, 5 and 6 were also identified as potent DPPH radical scavengers indicating that their potent anti-AGEs activities might be, at least in part, related to antioxidant action. It has however been noted that, in the

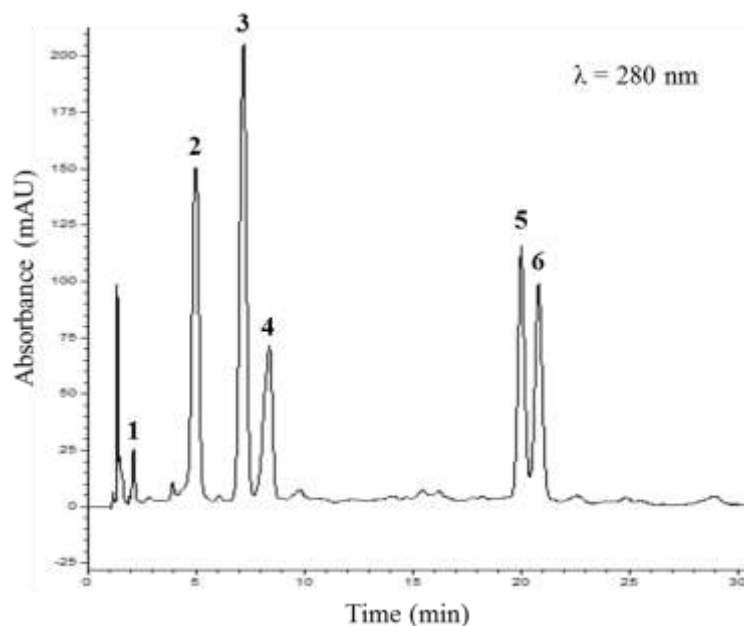


Figure 1. HPLC-UV Profile of Butanol Fraction from *Mangifera indica* methanol extract with Detection at 280 nm. **1.** Gallic acid; **2.** Iriflophenone 3-C-β-D-glucoside; **3.** Mangiferin; **4.** Iriflophenone 3-C-(2'-O-galloyl)-β-D-glucoside; **5.** Hyperoside; **6.** Isoquercitrin.

Table 2. UV and MS Data of Major Constituents of Butanol Fraction from *Mangifera indica* methanol extract.

Compound	R _T (min)	[M - H] ⁻ (m/z)	MS ² fragment ions (m/z) ^a	λ _{max} ^b (nm)
Gallic acid (1)	2.1	169.0132	125	216 , 271
Iriflophenone 3-C-β-D-glucoside (2)	5.4	407.0980	317, 287 , 245, 193	207 , 295
Mangiferin (3)	7.2	421.0775	331, 301 , 271	240, 257 , 318, 365
Iriflophenone 3-C-(2'-O-galloyl)-β-D-glucoside (4)	8.4	559.1091	407, 287 , 269, 169	208 , 284
Hyperoside (5)	20.2	463.0883	300 , 271	255, 353
Isoquercitrin (6)	20.9	463.0885	300 , 271	255, 353

Retention times (R_T), parent ions ([M - H]⁻) and UV maximum absorption (λ_{max}). ^aThe major ions are indicated in bold. ^bThe wavelengths of maximum absorption are indicated in bold.

same way as for fractions evaluation, no perfect correlation occurs between antioxidant and antiglycation activities of the studied constituents ($R^2 = 0.4592$). For instance, compound 1 was identified as the most potent DPPH scavenger of the fraction but was only inducing moderate antiglycation activity compared to compounds 3, 4, 5 and 6. It suggests thus that other mechanisms than antioxidant effect might account for the antiglycation properties of the most potent inhibitors constituents of *M. indica* leaves.

The formation of AGEs is indeed considered as a multifactorial process (Abdallah et al., 2016). Generated through several different pathways including Maillard reaction as well as glucose autoxidation, lipid peroxidation

or the polyol pathway, α-dicarbonyl species such as glyoxal (GO) and methylglyoxal (MGO) have also been identified as crucial intermediates in the formation of AGEs (Nowotny et al., 2015). It is now well established that scavenging these highly reactive carbonyl species constitute an effective strategy for limiting AGEs formation (Li et al., 2014). Of interest, several flavonoid derivatives including quercetin have been shown to efficiently trap GO and MGO under physiological conditions (Li et al., 2014). It is worth mentioning that A ring of quercetin was identified as a crucial structural feature for activity. Indeed, characterization of its MGO adducts proved that positions 6 and 8 of quercetin were the active sites for trapping dicarbonyl derivatives. To the

Table 3. AGEs inhibition and antioxidant activities of major constituents of butanol fraction from *Mangifera indica* methanol extract.

Compound	AGEs inhibition activity	DPPH scavenging activity
	IC ₅₀ (µM)	IC ₅₀ (µM)
1	279 ± 46	6.67 ± 0.24
2	334 ± 14	128 ± 6
3	101 ± 2	10.5 ± 0.3
4	217 ± 16	10.1 ± 0.1
5	102 ± 2	7.20 ± 0.2
6	89.2 ± 5.2	8.82 ± 0.5
Aminoguanidine	3 496 ± 94	ND

1. Gallic acid; 2. Iriflophenone 3-C-β-D-glucoside; 3. Mangiferin; 4. Iriflophenone 3-C-(2'-O-galloyl)-β-D-glucoside; 5. Hyperoside; 6. Isoquercitrin. ND, Not determined.

best of our knowledge, no data are available concerning hyperoside (5) and isoquercitrin (6). However, these two quercetin-3-O-glycosides possess the exact same A ring than quercetin and might also be capable of reacting with carbonyl species. By contrast, gallic acid (1) has been previously shown to exert almost no trapping effect of MGO (Shao et al., 2014). The lack of reactivity of that phenolic acid towards reactive dicarbonyl species could thus explain, at least in part, the modest antiglycation activity of compound 1 compared to flavonoid derivatives of the studied extract.

Conclusion

The present results attest that the leaves of *M. indica* exert strong and promising *in vitro* antiglycative activity. Further investigations using *in vivo* models would now be of major interest to confirm the potential of *M. indica* leaves to prevent carbonyl stress-related diseases. By using a bio-guided approach, this study also identified six potent antiglycative constituents including gallic acid, mangiferin, quercitrin, hyperoside, iriflophenone 3-C-β-D-glucoside and iriflophenone 3-C-(2'-O-galloyl)-β-D-glucoside. With IC₅₀ values lower than that of aminoguanidine, these six phenolic compounds can be regarded as remarkable inhibitors of AGEs formation as well as suitable markers for quality control of mango leaves.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

REFERENCES

Abdallah HM, El-Bassosy H, Mohamed GA, El-Halawany AM, Alshali KZ, Banjar ZM (2016). Phenolics from *Garcinia mangostana* inhibit advanced glycation endproducts formation: effect on Amadori

products, cross-linked structures and protein thiols. *Molecules* 21(2):251.

Abdallah HM, El-Bassosy HM, Mohamed GA, El Halawany AM, Alshali KZ, Banjar ZM (2017). Mangostana xanthenes III and IV: advanced glycation end-product inhibitors from the pericarp of *Garcinia mangostana*. *Journal of Natural Medicines* 71(1):216-226.

Barreto JC, Trevisan MTS, Hull WE, Erben G, DE Brito ES, Pfundstein B, Würtele G, Spiegelhalter B, Owen RW (2008). Characterization and Quantitation of Polyphenolic Compounds in Bark, Kernel, Leaves, and Peel of Mango (*Mangifera indica* L.). *Journal of Agricultural and Food Chemistry* 56(14):5599-5610.

Brings S, Fleming T, Freichel M, Muckenthaler MU, Hergiz S, Nawroth PP (2017). Dicarbonyls and advanced glycation end-products in the development of diabetic complications and targets for intervention. *International Journal of Molecular Sciences* 18(1):1-24.

Derbré S, Gatto J, Pelleray A, Coulon L, Séraphin D, Richomme P (2010). Automating a 96-well microtiter plate assay for identification of AGEs inhibitors or inducers: application to the screening of a small natural compounds library. *Analytical and bioanalytical chemistry* 398(4):1747-1758.

Fernández-Ponce MT, Casas L, Mantell C, Rodríguez M, De la Ossa EM (2012). Extraction of antioxidant compounds from different varieties of *Mangifera indica* leaves using green technologies. *The Journal of Supercritical Fluids* 72:168-175.

Fernández-Ponce MT, Casas L, Mantell C, De la Ossa EM (2015). Use of high pressure techniques to produce *Mangifera indica* L. leaf extracts enriched in potent antioxidant phenolic compounds. *Innovative Food Science and Emerging Technologies* 29:94-106.

Halake K, Birajdar M, Lee J (2016). Structural implications of polyphenolic antioxidants. *Journal of Industrial and Engineering Chemistry* 35:1-7.

Itoh K, Murata K, Sakaguchi N, Akai K, Yamaji T, Shimizu K, Isaki K, Matsukawa T, Kajiyama S, Fumuro M, Iijima M, Matsuda H (2017). Inhibition of advanced glycation end products formation by *Mangifera indica* leaf extract. *Journal of Plant Studies* 6(2):102-107. <http://www.ccsenet.org/journal/index.php/jps/article/view/68927>

Kim CS, Park S, Kim J (2017). The role of glycation in the pathogenesis of aging and its prevention through herbal products and physical exercise. *Journal of Exercise Nutrition and Biochemistry* 21:55-61.

Kim HK, Lee JM, Yokozawa T, Sakata K, Lee S (2011). Protective activity of flavonoid and flavonoid glycosides against glucose-mediated protein damage. *Food Chemistry* 126:892-895.

Li X, Zheng T, Sang S, Lv L (2014). Quercetin inhibits advanced glycation end product formation by trapping methylglyoxal and glyoxal. *Journal of Agricultural and Food Chemistry* 62:12152-12158.

Ling LT, Yap S, Radhakrishnan AK, Subramaniam T, Cheng HM, Palanisamy UD (2009). Standardised *Mangifera indica* extract is an ideal antioxidant. *Food Chemistry* 113:1154-1159.

Meda NR, Fraisse D, Gnoula C, Vivier M, Felgines C, Senejoux F (2017). Characterization of antioxidants from *Detarium microcarpum*

- Guill. et Perr. leaves using HPLC-DAD coupled with pre-column DPPH assay. *European Food Research and Technology* 243:1659-1666.
- Mildner-Szkudlarz S, Siger A, Szwengiel A, Przygonski K, Wojtowicz E, Zawirska-Wojtasiak R (2017). Phenolic compounds reduce formation of N ϵ -(carboxymethyl)lysine and pyrazines formed by Maillard reactions in a model bread system. *Food Chemistry* 231:175-184.
- Nowotny K, Jung T, Höhn A, Weber D, Grune T (2015). Advanced glycation end products and oxidative stress in type 2 diabetes mellitus. *Biomolecules* 5:194-222.
- Pereira CG, Meireles MAA (2007). Evaluation of global yield, composition, antioxidant activity and cost of manufacturing of extracts from lemon verbena (*Aloysia triphylla* [L'herit.] Britton) and mango (*Mangifera indica* L.) leaves. *Journal of Food Process Engineering* 30:150-173.
- Pranakhon R, Aromdee C, Pannangpetch P (2015). Effects of iriflophenone 3-C- β -glucoside on fasting blood glucose level and glucose uptake. *Pharmacognosy Magazine* 11:82-89.
- Reddy VP, Beyaz A (2006). Inhibitors of the Maillard reaction and AGE breakers as therapeutics for multiple diseases. *Drug Discovery Today* 11:646-654.
- Rodeiro I, Cancino L, González JE, Morffi J, Garrido G, González RM, Nuñez A, Delgado R (2006). Evaluation of the genotoxic potential of *Mangifera indica* L. extract (Vimang), a new natural product with antioxidant activity. *Food and Chemical Toxicology* 44:1707-1713.
- Shaheen N, Lu Y, Geng P, Shao Q, Wei Y (2017). Isolation of four phenolic compounds from *Mangifera indica* L. flowers by using normal phase combined with elution extrusion two-step high speed countercurrent chromatography. *Journal of Chromatography B* 1046:211-217.
- Shao X, Chen H, Zhu Y, Sedighi R, Ho CT, Sang S (2014). Essential structural requirements and additive effects for flavonoids to scavenge methylglyoxal. *Journal of Agricultural and Food Chemistry* 62:3202-3210.
- Vasil'ev SA, Garazd MM, Khilya VP (2006). 3-Phenoxychromones: Natural distribution, synthetic and modification methods, biological properties. *Chemistry of Natural Compounds* 42:241-253.
- Yakubu MT, Salimon SS (2015). Antidiarrhoeal activity of aqueous extract of *Mangifera indica* L. leaves in female albino rats. *Journal of Ethnopharmacology* 163:135-141.
- Yang R, Wang WX, Chen HJ, He ZC, Jia AQ (2018). The inhibition of advanced glycation end-products by five fractions and three main flavonoids from *Camellia nitidissima* Chi flowers. *Journal of Food and Drug Analysis* 26:252-259.

Related Journals:

