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Published International Scientific Research 2023

October 2023

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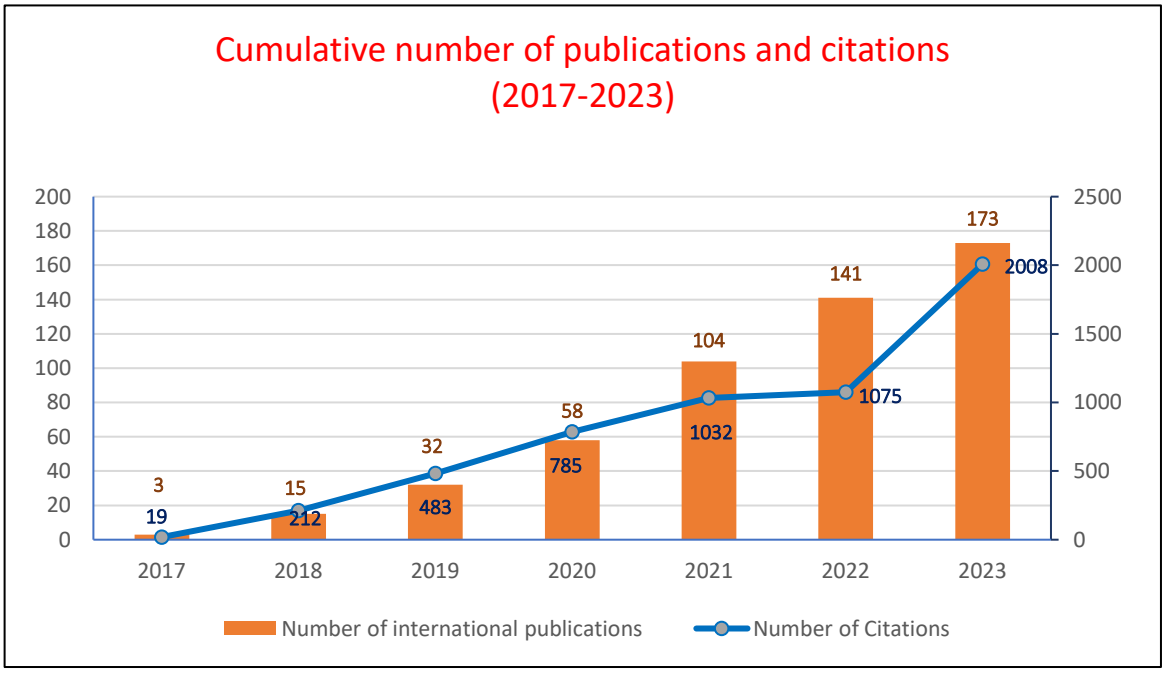
PUBLICATION STATISTICS

1. Number of international publications and citations with NGU affiliation per year

Year	International publications	Citations
2023	32	33
2022	37	43
2021	46	247
2020	26	302
2019	17	271
2018	12	193
2017	3	19
Total	173	2005



2. The ratio of SOP international publications to staff members (2017-2023)

Year of publication	International publications	Staff members	The ratio
2023	32	16	2
2022	37	13	2.84
2021	46	12	3.83
2020	26	12	2.17
2019	17	10	1.7
2018	12	6	2
2017	3	3	1

3. International publications with highest impact factor (5 and above) in 2023

No.	Publications	IF
1.	• Therapeutic effects of combining curcumin and swimming in osteoarthritis using a rat model. • Biomedicine and Pharmacotherapy. • **Dr. Reham Essam**	7.5
2.	• Potent Dual Inhibitors of Steroid Sulfatase and 17βHydroxysteroid Dehydrogenase Type 1 with a Suitable Pharmacokinetic Profile for In Vivo Proof-of-Principle Studies in an Endometriosis Mouse Model. • J. Medicinal Chemistry. • **Dr. Mohamed Salah**	7.3
3.	• Exploring novel anticancer pyrazole benzenesulfonamides featuring tail approach strategy as carbonic anhydrase inhibitors. • European Journal of Medicinal Chemistry. • **Prof. Marwa Fuoad**	6.7
4.	• Unleashing lactoferrin's antidepressant potential through the PI3K/Akt/mTOR pathway in chronic restraint stress rats**.** • Food and Function. • **A/prof. Ayman El-Sahar and Dr. Reham Essam**	6.1
5.	• Targeting HMGB1/PI3K/Akt and NF-κB/Nrf-2 signaling pathways by vildagliptin mitigates testosterone-induced benign prostate hyperplasia in rats. • Life Sciences. • **Prof. Rania M. Abdelsalam, A/prof. Ayman El-Sahar and Dr. Reham Essam, and TA/ Noha Eisaa**	6.1
6.	• The citrus flavonoid "Nobiletin" impedes STZ-induced Alzheimer's disease in a mouse model through regulating autophagy mastered by SIRT1/FoxO3a mechanism. • Inflammopharmacology. • **Dr. Reham Essam**	5.8
7.	• Dual-target ligand discovery for Alzheimer's disease: triphenylphosphoranylidene derivatives as inhibitors of acetylcholinesterase and β-amyloid aggregation. • Journal of Enzyme Inhibition and Medicinal Chemistry • **Prof. Marwa Fuoad**	5.75
8.	• Immunogenicity of CRISPR therapeutics—Critical considerations for clinical translation. • Frontiers in Bioengineering and Biotechnology. • **Dr. Radwa Ewaisha.**	5.7

No.	Publications	IF
9.	• Implication of Wnt/GSK-3β/β-Catenin Signaling in the Pathogenesis of Mood Disturbances Associated with Hyperthyroidism in Rats: Potential Therapeutic Effect of Naringin. • ACS Chem Neurosci. • **Dr. Reham Essam**	5.7
10.	• Donepezil halts acetic acid-induced experimental colitis in rats and its associated cognitive impairment through regulating inflammatory/oxidative/apoptotic cascades: An add-on to its anti-dementia activity. • Int. Immunopharmacology. • **Dr. Reham Essam**	5.6
11.	• Cubosomal-functionalized block copolymer platform for dual delivery of linagliptin and empagliflozin: Recent advances in synergistic strategies for maximizing control of high-risk type II diabetes • Drug Delivery and Translational Research. • **Prof. Nevine Shawky**	5.4
12.	• p-CREB and p-DARPP-32 orchestrating the modulatory role of cAMP/PKA signaling pathway enhanced by Roflumilast in rotenone-induced Parkinson's disease in rats. • ChemicoBiological Interaction. • **Dr. Reham Essam**	5.2
13.	• Novel benzenesulfonamide-thiouracil conjugates with a flexible N-ethyl acetamide linker as selective CA IX and CA XII inhibitors. • Arch Pharm (Weinheim) • **A/Prof. Ahmed Elkerdawy**	5.1
14.	• Novel 2-oxo-2-phenylethoxy and benzyloxy diaryl urea hybrids as VEGFR-2 inhibitors: Design, synthesis, and anticancer evaluation. • Arch Pharm (Weinheim) • **A/Prof. Ahmed Elkerdawy**	5.1
15.	• Novel VEGFR-2 inhibitors as antiangiogenic and apoptotic agents via paracrine and autocrine cascades: Design, synthesis, and biological evaluation. • Bioorganic Chemistry. • **Prof. Marwa Fouad**	5.1
16.	• New quinazolinone-based derivatives as DHFR/EGFR-TK inhibitors: Synthesis, molecular modeling simulations, and anticancer activity. • Arch Pharm (Weinheim) • **A/Prof. Ahmed Elkerdawy**	5.1

No.	Publications	IF
17.	• LncRNA NEAT1 and MALAT1 are involved in polycystic ovary syndrome pathogenesis by functioning as competing endogenous RNAs to control the expression of PCOS-related target genes. • Noncoding RNA Research • **Dr. Sally Atef Fahim**	5

SCHOOL OF PHARMACY INTERNATIONAL PUBLICATIONS 2023

173 International publications were published with NGU affiliation throughout the period from January 2017 to October 2023

Impact factors and number of citations of publications per scientific department

Department of Chemistry			
Total number of publications (2023)	13	Total number of citations (2023)	12

Serial	Publications	IF	Citations
1.	Iman AY Ghannam, **Ahmed M El Kerdawy**, Marwa M Mounier, Mahmoud T Abo-Elfadl, Islam H Ali. Novel 2-oxo-2-phenylethoxy and benzyloxy diaryl urea hybrids as VEGFR-2 inhibitors: Design, synthesis, and anticancer evaluation. Arch Pharm (Weinheim) (**2023**) Feb;356(2):e2200341. **doi: 10.1002/ardp.202200341**	5.1	1
2.	Heba T Abdel-Mohsen, **Ahmed M El Kerdawy**, Andrea Petreni, Claudiu T Supuran. Novel benzenesulfonamide-thiouracil conjugates with a flexible N-ethyl acetamide linker as selective CA IX and CA XII inhibitors. Arch Pharm (Weinheim) (**2023**) Feb;356(2):e2200434. **doi: 10.1002/ardp.202200434**	5.1	1
3.	Yomna I El-Gazzar, Heba R Ghaiad, **Ahmed M El Kerdawy**, Riham F George, Hanan H Georgey, Khairia M Youssef, Hussein I El-Subbagh. New quinazolinone-based derivatives as DHFR/EGFR-TK inhibitors: Synthesis, molecular modeling simulations, and anticancer activity. Arch Pharm (Weinheim) (**2023**) Jan;356(1):e2200417. **doi: 10.1002/ardp.202200417**	5.1	3
4.	**Salah, M.;** Tahoun, M.; Rudzitis-Auth, J.; Stotz, L.; van Koppen, C. J.; Laschke, M. W.; Abdelsamie, A. S.; Frotscher, M. Potent Dual Inhibitors of Steroid Sulfatase and 17βHydroxysteroid Dehydrogenase Type 1 with a Suitable Pharmacokinetic Profile for In Vivo Proof-of-Principle Studies in an Endometriosis Mouse Model. J. Med. Chem. 2023, 66 (13), 8975–8992. doi: 10.1021/acs.jmedchem.3c00571.	7.3	0

Department of Chemistry			
5.	El-Hussieny, M., Abd-El-Maksoud, M.A., Soliman, F.M., **Fouad, M.A.,** El-Ashrey, M.K. Dual-target ligand discovery for Alzheimer's disease: triphenylphosphoranylidene derivatives as inhibitors of acetylcholinesterase and β-amyloid aggregation. Journal of Enzyme Inhibition and Medicinal Chemistry, (**2023**) 38 (1), art. no. 2166040. **doi: 10.1080/14756366.2023.2166040**.	5.6	1
6.	Ola Ahmed Saleh, Amr Mohamed Badawey, Hassan Y. Aboul Enein and **Marwa Ahmed Fouad**. Enantioseparation, quantification, molecular docking and molecular dynamics study of five β adrenergic blockers on Lux Cellulose 2 column. BMC Chemistry, (**2023**) 17 (1), art. no. 22. **doi: 10.1186/s13065-023-00925-2**.	4.6	0
7.	Salem, W.A., Elkady, E.F., **Fouad, M.A.,** Mohammad, M.A.-A. DoE Screening and Optimization of Liquid Chromatographic Determination of Nicotinic Acid and Six Statins: Application to Pharmaceutical Preparations and Counterfeit Detection. Journal of chromatographic science, (**2023**) 61 (1), pp. 74-86. **doi: 10.1093/chromsci/bmab131**.	1.3	2
8.	Abdel Rahman, D.E., **Fouad, M.A**., Mohammed, E.R., El-Zoheiry, H.H., Abdelrasheed Allam, H. Novel VEGFR-2 inhibitors as antiangiogenic and apoptotic agents via paracrine and autocrine cascades: Design, synthesis, and biological evaluation. Bioorg. Chem. **(2023**) 139, 106678. **doi: 10.1016/j.bioorg.2023.106678.**	5.1	0
9.	Ezzat, M.A.F., Abdelhamid, S.M., **Fouad, M.A**., Abdel-Aziz, H.A., Allam, H.A. Design, synthesis, in vitro, and in vivo evaluation of novel phthalazinone-based derivatives as promising acetylcholinesterase inhibitors for treatment of Alzheimer's disease. Drug Development Research, (**2023**) 84(6), pp. 1231–1246. **doi: 10.1002/ddr.22082.**	3.8	0
10.	Ezzat, M.A.F., Elmasry, G.F., El-Mageed, M.M.A.A., **Fouad, Marwa** A., Abdel-Aziz, H.A., Elewa, S.I. Design, synthesis, and biological evaluation of furan-bearing pyrazolo[3,4-b]pyridines as novel inhibitors of CDK2 and P53–MDM2	3.8	0

Department of Chemistry			
	protein–protein interaction. Drug Development Research, (2023) 84(6), pp. 1183–1203 doi: 10.1002/ddr.22079		
11.	Ahmed, R.F., Mahmoud, W.R., Abdelgawad, N.M., **Fouad, M.A.**, Said, M.F. Exploring novel anticancer pyrazole benzenesulfonamides featuring tail approach strategy as carbonic anhydrase inhibitors. European Journal of Medicinal Chemistry, (2023) 261, 115805. doi: 10.1016/j.ejmech.2023.115805.	7.1	0
12.	Ehab Elkady, **Marwa Fouad**, Ayoub Mozayad. Application of Box–Behnken Design and Response Surface Methodology for Selecting the Optimum RP-HPLC Conditions for the Simultaneous Determination of Paracetamol and Diclofenac Sodium Along With Three Skeletal Muscle Relaxants in Three Different Pharmaceutical Dosage Forms. Journal of chromatographic science, (2023) In press. doi: doi.org/10.1093/chromsci/bmad051	1.3	2
13.	Rania S M Ismail, **Ahmed M El Kerdawy**, Dalia H Soliman, Hanan H Georgey, Nagwa M Abdel Gawad, Andrea Angeli, Claudiu T Supuran. Discovery of a new potent oxindole multi-kinase inhibitor among a series of designed 3-alkenyl-oxindoles with ancillary carbonic anhydrase inhibitory activity as antiproliferative agents. BMC Chem (2023) 18;17(1):81. doi: 10.1186/s13065-023-00994-3	4.6	1

Department of Biology			
Total number of publications (2023)	17	Total number of citations (2023)	21

Serial	Publications	IF	Citations
1.	**Fahim SA**, Ibrahim S, Tadros SA, Badary OA. Protective effects of butylated hydroxytoluene on the initiation of N-nitrosodiethylamine-induced hepatocellular carcinoma in albino rats. Hum Exp Toxicol. (2023) Jan-Dec; 42:9603271231165664.	2.8	1

	doi: 10.1177/09603271231165664.		
2.	Badr AM, Elkholy O, Said M, **Fahim SA**, El-Khatib M, Sabry D, Gaber RM. Diagnostic significance of hsa_circ_0000146 and hsa_circ_0000072 biomarkers for Diabetic Kidney Disease in patients with type 2 diabetes mellitus. J Med Biochem. (**2023**) Mar 15;42(2):239-248. **doi: 10.5937/jomb0-39361.**	2.5	0
3.	ElMonier AA, El-Boghdady NA, **Fahim SA**, Sabry D, Elsetohy KA, Shaheen AA. LncRNA NEAT1 and MALAT1 are involved in polycystic ovary syndrome pathogenesis by functioning as competing endogenous RNAs to control the expression of PCOS-related target genes. Noncoding RNA Res. (**2023**) Mar 3;8(2):263-271. **doi: 10.1016/j.ncrna.2023.02.008.**	5	2
4.	Shimaa Abdelsattar *, **Sally A. Fahim**, Hiba S Al-Amodi, Hala F.M. Kamel, Zeinab A. Kasemy, Fatma O. Khalil, Mahmoud S. Abdallah, Hanan M Bedair, Abd El-Naser Abd El-Ati Gad Alla, Alyaa Sabry, Mohamed A. Sakr, Mahmoud Selim, Eman M. Abd Elgayed. The Potential Role of Circulating Long miscellaneous RNAs in the Diagnosis and Prognosis of hepatitis C related Hepatocellular Carcinoma. Non-Coding RNA. (**2023**)	4.5	0
5.	**Ewaisha, R.,** & Anderson, K. S. Immunogenicity of CRISPR therapeutics—Critical considerations for clinical translation. Frontiers in Bioengineering and Biotechnology**. 2023**, volume 11. **doi:10.3389/fbioe.2023.1138596**	5.7	5
6.	Mariam Omara, Mohamed Hagras, Mohamed M Elsebaie, Nader S Abutaleb, Hanzada T Nour El-Din, Maria O Mekhail, **Ahmed S Attia**, Mohamed N Seleem, Marwa T Sarg, Abdelrahman S Mayhoub. Exploring novel aryl/heteroaryl-isosteres of phenylthiazole against multidrug-resistant bacteria. RSC Adv. (**2023**) Jul 6;13(29):19695-19709. **doi: 10.1039/d3ra02778c**.	3.9	1
7.	El-Din, H.T.N.; Elsebaie, M.M.; Abutaleb, N.S.; Kotb, A.M.; **Attia, A.S.**; Seleem, M.N.; Mayhoub, A.S. Expanding the structure–activity relationships of alkynyl diphenylurea	4.1	1

	scaffold as promising antibacterial agents. RSC Medicinal Chemistry (**2023**), 14, 367-377. **doi:10.1039/D2MD00351A**		
8.	Hebatollah E Eitah, Hanan Naeim Attia, Ahmed A F Soliman, Amina A Gamal El Din, Khaled Mahmoud, Rabab H Sayed, Yousreya A Maklad, Ayman E El-Sahar. Vitamin D ameliorates diethylnitrosamine-induced liver preneoplasia: A pivotal role of CYP3A4/CYP2E1 via DPP-4 enzyme inhibition. Toxicol Appl Pharmacol. (**2023**) 1:458:116324. **doi: 10.1016/j.taap.2022.116324.**	3.8	0
9.	**Essam, R.M**., Saadawy, M.A., **Gamal, M., Abdelsalam, R.M**., **El-Sahar, A.E**. Lactoferrin averts neurological and behavioral impairments of thioacetamide-induced hepatic encephalopathy in rats via modulating HGMB1/TLR-4/MyD88/Nrf2 pathway. Neuropharmacology, (**2023**), 236, 109575. **doi: 10.1016/j.neuropharm.2023.109575**	4.7	0
10.	**El-Sahar, A.E.,** Bekhit, N.**, Eissa, N.M., Abdelsalam, R.M., Essam, R.M.** Targeting HMGB1/PI3K/Akt and NF-κB/Nrf-2 signaling pathways by vildagliptin mitigates testosterone-induced benign prostate hyperplasia in rats. Life Sciences, (**2023**), 322, 121645 **doi: 10.1016/j.lfs.2023.121645.**	6.1	2
11.	Abdalhameid, E., Abd El-Haleim, E.A**., Abdelsalam, R.M.,** Fawzy, H.M., Kenawy, S.A. Cinnamic acid mitigates methotrexate-induced lung fibrosis in rats: comparative study with pirfenidone. Naunyn-Schmiedeberg's Archives of Pharmacology, **(2023).** **doi: 10.1007/s00210-023-02652-w.**	3.6	0
12.	Mai A Abd-Elmawla, **Reham M Essam**, Kawkab A Ahmed, Maha Abdelmonem. Implication of Wnt/GSK-3β/β-Catenin Signaling in the Pathogenesis of Mood Disturbances Associated with Hyperthyroidism in Rats: Potential Therapeutic Effect of Naringin. ACS Chem Neurosci. (**2023**);14(11):2035-2048. **doi: 10.1021/acschemneuro.3c00013.**	5.7	4

13.	Eman M Elbaz, **Reham M Essam**, Kawkab A Ahmed, Maheera H Safwat. Donepezil halts acetic acid-induced experimental colitis in rats and its associated cognitive impairment through regulating inflammatory/oxidative/apoptotic cascades: An add-on to its anti-dementia activity. Int Immunopharmacol. (**2023**), 116:109841. **doi: 10.1016/j.intimp.2023.109841**	**5.6**	**4**
14.	**Reham M Essam**, Esraa A Kandil. p-CREB and p-DARPP-32 orchestrating the modulatory role of cAMP/PKA signaling pathway enhanced by Roflumilast in rotenone-induced Parkinson's disease in rats. Chem Biol Interact. (**2023**) 25:372:110366. **doi: 10.1016/j.cbi.2023.110366**	**5.1**	**1**
15.	Mona M Saber, Manal Moustafa Mahmoud, Hesham M Amin, **Reham M Essam**. Therapeutic effects of combining curcumin and swimming in osteoarthritis using a rat model. Biomed Pharmacother. (**2023**) 166:115309. **doi: 10.1016/j.biopha.2023.115309.**	**7.5**	**0**
16.	Shohda A El-Maraghy, Aya Reda, **Reham M Essam**, Mona A Kortam. The citrus flavonoid "Nobiletin" impedes STZ-induced Alzheimer's disease in a mouse model through regulating autophagy mastered by SIRT1/FoxO3a mechanism. Inflammopharmacology (**2023**);31(5):2701-2717. **doi: 10.1007/s10787-023-01292-z.**	**5.8**	**0**
17.	Hanan H. Ahmed, **Reham M. Essam**, Muhammed F. El-Yamany, Kawkab A. Ahmed and **Ayman E. El-Sahar**. Unleashing Lactoferrin's antidepressant potential through the PI3K/Akt/mTOR pathway in chronic restrain stress rats. Food Funct. **2023** **doi: 10.1039/d3fo02222f.**	6.1	0

Department of Pharmaceutics and Industrial Pharmacy			
Total number of publications (2023)	2	Total number of citations (2023)	0

Serial	Publications	IF	Citations
1.	Reham Hammad, Rania Sanad, **Nevine S. Abd El Malak**, Randa Latif. Cubosomal-functionalized block copolymer platform for dual delivery of linagliptin and empagliflozin: Recent advances in synergistic strategies for maximizing control of high-risk type II diabetes. Drug Delivery and Translational Research. (**2023**) doi: 10.1007/s13346-023-01423-7	5. 4	0
2.	Sandy N Aziz , Alia A Badawy , Demiana I Nessem , **Nevine S Abd El Malak** , Marianne J Naguib. Chitosan-coated alginate (CCA) nanoparticles for augmentation of topical antihistaminic activity of diphenhydramine: in-vitro optimization, skin histopathology and pharmacodynamic studies with in vitro/in vivo correlation. Drug development &industrial pharmacy. (**2023)** Apr;49(4):316-327. doi: 10.1080/03639045.2023.2211672	3.4	0

SCHOOL OF PHARMACY INTERNATIONAL PUBLICATIONS 2022

32 International publications with NGU affiliation published in 2023 with 33 citations.

No.	Publication	IF	Citations
1.	Iman AY Ghannam, **Ahmed M El Kerdawy**, Marwa M Mounier, Mahmoud T Abo-Elfadl, Islam H Ali. "Novel 2-oxo-2-phenylethoxy and benzyloxy diaryl urea hybrids as VEGFR-2 inhibitors: Design, synthesis, and anticancer evaluation." Arch Pharm (Weinheim) (**2023**) 356(2): e2200341. DOI:10.1002/ardp.202200341	5.1	1

Abstract

Two series of diaryl urea derivatives, 6a–k and 7a–n, were synthesized. All the newly synthesized compounds were tested against the NCI (US) cancer cell lines via SRB assay. The p-chloro-m-trifluoromethyl phenyl derivatives 6e–g and 7e–g showed the most potent cytotoxic activity with a GI50 value range of 1.2–15.9 µM. Furthermore, the p-fluorobenzyloxy diaryl urea derivative 7g revealed the most potent cytotoxicity against eight cancer cell lines in the MTT assay with IC50 values below 5 µM. Compounds 6a–k and 7a–n were tested for their vascular endothelial growth factor receptor-2 (VEGFR-2) kinase inhibitory activities. The p-chloro-m-trifluoromethyl diaryl urea benzyloxy derivatives 7e–i and the p-methoxydiaryl urea benzyloxy derivatives 7k, 7l, and 7n were found to be the most active compounds as VEGFR-2 inhibitors in the benzyloxy series 7, with an IC50 range of 0.09–4.15 µM. In the 2-oxo-2-phenylethoxy series 6, compounds 6e–g and 6i were reported with IC50 values of 0.94, 0.54, 2.71, and 4.81 µM, respectively. Moreover, compounds 7e and 7g induced apoptosis, causing cell cycle arrest in the G2/M phase. In addition, 7g showed an antimigratory effect in A-375 cells and inhibited the VEGFR-2 expression in an immunohistofluorescence study. Molecular docking simulations on VEGFR-2 as well as ADME properties prediction were also performed.

No.	Publication	IF	Citations
2.	Rania S M Ismail, **Ahmed M El Kerdawy**, Dalia H Soliman, Hanan H Georgey, Nagwa M Abdel Gawad, Andrea Angeli, Claudiu T Supuran. "Discovery of a new potent oxindole multi-kinase inhibitor among a series of designed 3-alkenyl-oxindoles with ancillary carbonic anhydrase inhibitory activity as antiproliferative agents", BMC Chem (**2023**) 18;17(1):81 DOI: 10.1186/s13065-023-00994-3	4.6	2

Abstract

An optimization strategy was adopted for designing and synthesizing new series of 2-oxindole conjugates. Selected compounds were evaluated for their antiproliferative effect in vitro against NCI-60 cell lines panel, inhibitory effect on carbonic anhydrase (CA) isoforms (hCAI, II, IX and XII), and protein kinases. Compounds 5 and 7 showed promising inhibitory effects on hCA XII, whereas compound 4d was the most potent inhibitor with low nanomolar CA inhibition against all tested isoforms. These results were rationalized by using molecular docking. Despite its lack of CA inhibitory activity, compound 15c was the most active antiproliferative candidate against most of the 60 cell lines with mean growth inhibition 61.83% and with IC50 values of 4.39, 1.06, and 0.34 nM against MCT-7, DU 145, and HCT-116 cell lines, respectively. To uncover the mechanism of action behind its antiproliferative activity, compound 15c was assessed against a panel of protein kinases (RET, KIT, cMet, VEGFR1,2, FGFR1, PDFGR and BRAF) showing % inhibition of 74%, 31%, 62%, 40%, 73%, 74%, 59%, and 69%, respectively, and IC50 of 1.287, 0.117 and 1.185 µM against FGFR1, VEGFR, and RET kinases, respectively. These results were also explained through molecular docking.

No.	Publication	IF	Citations
3.	Heba T Abdel-Mohsen, **Ahmed M El Kerdawy**, Andrea Petreni, Claudiu T Supuran "Novel benzenesulfonamide-thiouracil conjugates with a flexible N-ethyl acetamide linker as selective CA IX and CA XII inhibitors", *Arch* Pharm (Weinheim) **(2023)** 356(2): e2200434. DOI: 10.1002/ardp.202200434	5.1	1

Abstract:

Novel benzenesulfonamide derivatives linked to diverse functionalized thiouracils through a flexible N-ethyl acetamide linker were designed and synthesized as carbonic anhydrase (CA) inhibitors. The synthesized candidates demonstrated a potent inhibitory activity against four different CA isoforms in the nanomolar range. Compound 10d showed more than twofold higher potency than the reference AAZ against CA II with Ki of 5.65 and 12 nM, respectively. Moreover, compounds 10d and 20 revealed potent activity against CA IX with Ki of 18.1 and 14.2 nM, respectively. In addition, 10c, 10d, 11b, 11c, and 20 demonstrated high potency against the CA XII isozyme with a Ki range of 4.18-4.8 nM. Most of the synthesized derivatives displayed preferential selectivity toward the CA IX and CA XII isoforms over CA I and CA II. Compounds 11a and 20 exhibited favorable selectivity toward CA IX over CA II with a selectivity index (SI) of 14.36 and 16.62, respectively, and toward CA XII over CA II with SI of 71.01 and 51.19, respectively. Molecular docking simulations showed that the synthesized conjugates adopted comparable binding modes in the CA I, CA II, CA IX, and CA XII isoforms, involving the deep fitting of the sulfonamide moiety in the base of the CA active site via chelation of the Zn2+ ion and H-bond interaction with the key amino acids Thr199 and/or Thr200. Moreover, the N-ethyl acetamide flexible linker enables the substituted thiouracils and fused thiouracil tail to achieve multiple interactions with the surrounding hydrophobic and hydrophilic regions.

No.	Publication	IF	Citations
4.	Yomna I El-Gazzar, Heba R Ghaiad, **Ahmed M El Kerdawy**, Riham F George, Hanan H Georgey, Khairia M Youssef, Hussein I El-Subbagh. "New quinazolinone-based derivatives as DHFR/EGFR-TK inhibitors: Synthesis, molecular modeling simulations, and anticancer activity." Arch Pharm (Weinheim) (**2023**) 356(1):e2200417. DOI: 10.1002/ardp.202200417	5.1	3

Abstract:

New 2-mercapto-quinazolin-4-one analogs were synthesized and tested for their in vitro anticancer activity, dihydrofolate reductase (DHFR) inhibition, and epidermal growth factor tyrosine kinase (EGFR-TK) inhibition activities. Compound 24, which is characterized by a 2-benzyl-thio function, showed broad-spectrum anticancer activity with high safety profile and selectivity index. The concentrations of 24 causing 50% growth inhibition (GI_{50}) and total cell growth inhibition (TGI) and its lethal concentration 50 (LC_{50}) were 15.1, 52.5, and 91.2 µM, respectively, using 5-fluorouracil as a positive control. Also, it showed EGFR-TK inhibitory activity with IC_{50} = 13.40 nM compared to gefitinib (IC_{50} = 18.14 nM) and DHFR inhibitory potency with 0.30 µM compared to methotrexate (MTX; IC_{50} = 0.08 µM). In addition, compound 24 caused cell cycle arrest and apoptosis on COLO-205 colon cancer cells. Compounds 37, 21, and 54 showed remarkable DHFR inhibitory activity with IC_{50} values of 0.03, 0.08, and 0.08 µM, respectively. The inhibitory properties of these compounds are due to an electron-withdrawing group on the quinazolinone ring, except for compound 54. In a molecular modeling study, compound 24 showed the same binding mode as gefitinib as it interacted with the amino acid Lys745 via π-π interaction. Compound 37 showed a similar binding mode as MTX through the binding interaction with Lys68, Asn64 via hydrogen bond acceptor, and Phe31 via arene-arene interaction. The obtained model and substitution pattern could be used for further development.

No.	Publication	IF	Citations
5.	**Salah, M.;** Tahoun, M.; Rudzitis-Auth, J.; Stotz, L.; van Koppen, C. J.; Laschke, M. W.; Abdelsamie, A. S.; Frotscher, M. "Potent Dual Inhibitors of Steroid Sulfatase and 17βHydroxysteroid Dehydrogenase Type 1 with a Suitable Pharmacokinetic Profile for In Vivo Proof-of-Principle Studies in an Endometriosis Mouse Model." J. Med. Chem. (**2023**), 66 (13), 8975–8992. DOI: 10.1021/acs.jmedchem.3c00571	7.3	0

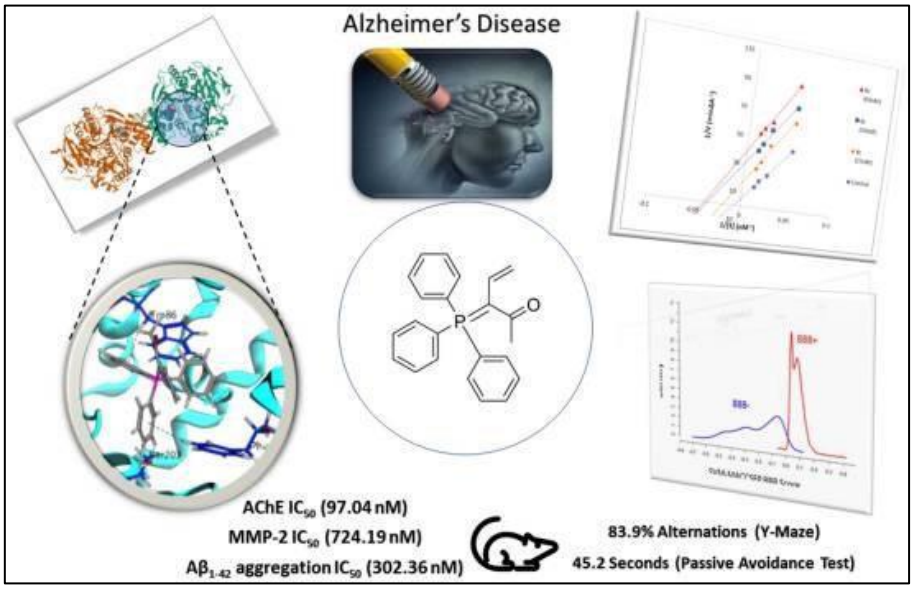
Abstract:

Treating estrogen-dependent diseases like endometriosis with drugs suppressing local estrogen activation may be superior to existing endocrine therapies. Steroid sulfatase (STS) and 17β-hydroxysteroid dehydrogenase type 1 (17β-HSD1) are key enzymes of local estrogen activation. We describe the rational design, synthesis, and biological profilation of furan-based compounds as a novel class of dual STS/17β-HSD1 inhibitors (DSHIs). In T47D cells, compound 5 showed irreversible inhibition of STS and potent, reversible inhibition of 17β-HSD1. It was selective over 17β-HSD2 and displayed high metabolic stabilities in human and mouse liver S9 fractions. No effect on cell viability was detected up to 31 µM (HEK293) and 23 µM (HepG2), respectively, and there was no activation of the aryl hydrocarbon receptor (AhR) up to 3.16 µM. Single daily application to mice revealed steady-state plasma levels high enough to make this compound eligible for an in vivo proof-of-principle study in a mouse endometriosis model.

No.	Publication	IF	Citations
6.	El-Hussieny, M., Abd-El-Maksoud, M.A., Soliman, F.M., **Fouad, M.A.,** El-Ashrey, M.K. "Dual-target ligand discovery for Alzheimer's disease: triphenylphosphoranylidene derivatives as inhibitors of acetylcholinesterase and β-amyloid aggregation." Journal of Enzyme Inhibition and Medicinal Chemistry, (2023) 38 (1), art. no. 2166040. DOI: 10.1080/14756366.2023.2166040	5.6	1

Abstract

Alzheimer disease (AD) is one of the major neurodegenerative diseases that could not be prevented or completely cured and may lead to death. Here, we target AChE and β-amyloid proteins. Synthesising new triphenylphosphporanylidene derivatives based on the surveyed literature and testing their biological activity revealed promising results especially for the acetyl triphenylphosphoranylidene derivative 8c, which showed good inhibitor activity against AChE enzyme with IC50 in the nanomolar range (97.04 nM); on the other hand, it showed poor selectivity for AChE versus butyrylcholinesterase but with some futural structural modification, this selectivity can be improved. 8c showed MMP-2 IC50 of 724.19 nM and Aβ1-42 aggregation IC50 of 302.36 nM. A kinetic study demonstrated that compound 8c uncompetitively inhibited AChE. Moreover, derivative 8c showed low cytotoxicity, good in vivo behavioural studies including Y-maze and passive avoidance tests with activity similar to that of donepezil. Finally, in silico studies for 8c predict its good penetration into BBB and good binding affinity in the AChE binding site.



No.	Publication	IF	Citations
7.	Ola Ahmed Saleh, Amr Mohamed Badawey, Hassan Y. Aboul Enein and **Marwa Ahmed Fouad**. "Enantioseparation, quantification, molecular docking and molecular dynamics study of five β adrenergic blockers on Lux Cellulose 2 column." BMC Chemistry, (**2023**) 17 (1), art. no. 22. DOI: 10.1186/s13065-023-00925-2	4.6	0

Abstract

Enantioseparation of five β-adrenergic blockers was studied using two mobile phases on a cellulose tris(3-chloro-4-methylphenylcarbamate) (Lux-Cellulose-2) chiral column in normal phase mode. The first mobile phase composed of n-hexane: ethanol: diethylamine 60: 40: 0.1 by volume has successfully resolved the chromatographic peaks of three pairs of β-adrenergic blockers namely, bisoprolol, carvedilol and atenolol. A mixture of n-hexane: ethanol: diethyl amine 75: 25: 0.1 by volume was used as the second mobile phase to separate the four pairs of enantiomers, metoprolol, carvedilol, nebivolol and atenolol with high resolution values. The mobile phases were pumped at a flow rate 1 mL/min with column temperature 25 °C using a UV detector at 230 nm. Molecular docking simulations of the five pairs of enantiomers was carried out in the cavities of the chiral stationary phase to gain a better understanding of the interaction between analyte enantiomers and chiral stationary phase and to better understand the mechanism of chiral recognition. According to the results, hydrogen bond interactions and π-π- interactions were the main types of interaction involved in the chiral recognition. Molecular dynamics simulation was performed to investigate the solvent effect on the interaction of the five pair of enantiomers in the chiral stationary phase cavity under dynamic conditions.

No.	Publication	IF	Citations
8.	Salem, W.A., Elkady, E.F., **Fouad, M.A.,** Mohammad, M.A.-A. "DoE Screening and Optimization of Liquid Chromatographic Determination of Nicotinic Acid and Six Statins: Application to Pharmaceutical Preparations and Counterfeit Detection." Journal of chromatographic science, (**2023**) 61 (1), pp. 74-86. DOI: 10.1093/chromsci/bmab131	1.3	2

Abstract

An isocratic reversed-phase high performance liquid chromatographic method has been developed and validated to simultaneously determine nicotinic acid, pravastatin sodium, rosuvastatin calcium, atorvastatin calcium, pitavastatin calcium, lovastatin sodium and simvastatin sodium in focus on counterfeit drug detection. Thin-layer chromatography, nuclear magnetic resonance and mass spectrometry have been additionally performed to verify the identification of adulterants of counterfeit herbal medicines. Chromatographic separation was carried out on Inertsil® ODS-3 C18 (4.6 × 150 mm, 5 µm) with isocratic mobile phase elution containing a mixture of acetonitrile: methanol: 25 mM potassium dihydrogen phosphate buffer, pH 2.86 adjusted with 0.1 M o-phosphoric acid (48: 30: 22, v/v/v), at a flow rate of 1 mL/min and with UV detection at 238 nm. The design of experiment methodology, Plackett-Burman and Box-Behnken designs, was used to screen and optimize the mobile phase composition. The validation of the method was also carried out under the International Conference on Harmonization guidelines. The developed method was sensitive, accurate, simple, economical and highly robust, in addition to the comprehensiveness and novelty of this method for separating the seven drugs. The results were statistically compared with the reference methods used Student's t-test and variance ratio F-test at $P < 0.05$..

No.	Publication	IF	Citations
9.	Abdel Rahman, D.E., **Fouad, M.A.,** Mohammed, E.R., El-Zoheiry, H.H., Abdelrasheed Allam, H. "Novel VEGFR-2 inhibitors as antiangiogenic and apoptotic agents via paracrine and autocrine cascades: Design, synthesis, and biological evaluation." Bioorg. Chem. (**2023**) 139, 106678. DOI: 10.1016/j.bioorg.2023.106678	5.1	0

Abstract

Appertaining to its paracrine and autocrine signaling loops, VEGFR-2 succeeded in grabbing attention as one of the leading targets in cancer treatment. Based on the foregoing and our comprehensive studies regarding pharmacophoric features and activity of sorafenib, novel phenylpyridazinone based VEGFR-2 inhibitors 4, 6a-e, 7a,b, 9a,b, 12a-c, 13a,b, 14a,b, 15a,b, and 17a-d were optimized. An assortment of biological assays was conducted to assess the antiangiogenic and apoptotic activities of the synthesized derivatives. In vitro VEGFR-2 kinase assay verified the inhibitory activity of the synthesized derivatives with IC50 values from 49.1 to 418.0 nM relative to the reference drug sorafenib (IC50 = 81.8 nM). Antiproliferative activity against HUVECs revealed that compounds 2-{2-[2-(6-oxo-3-phenylpyridazin-1(6H)-yl)acetyl]hydrazineyl}-N-(p-tolyl)acetamide (12c) and 2-[(5-mercapto-4-methyl-4H-1,2,4-triazol-3-yl)methyl]-6-phenylpyridazin-3(2H)-one (13a) possessed superior activity (IC50 values = 11.5 and 12.3 nM, respectively) in comparison to sorafenib (IC50 = 23.2 nM). For the purpose of appraising their antiproliferative effect, derivatives 12c and 13a were exposed to cell cycle analysis, apoptotic, cell invasion and migration assays in addition to determination of VEGFR-2 in protein level. Moreover, cytotoxicity as well as selectivity index against WI-38 cell line was measured to examine safety of derivatives 12c and 13a. After that, molecular docking study was executed on the top five compounds in the in vitro VEGFR-2 kinase assay 6d, 12c, 13a, 14a and 17c to get a deep perception on binding mode of the synthesized compounds and correlate the design strategy with biological results. Finally, physicochemical, pharmacokinetic properties, and drug-likeness studies were performed on the top five derivative in in vitro VEGFR-2 kinase assay.

No.	Publication	IF	Citations
10.	Ezzat, M.A.F., Abdelhamid, S.M., **Fouad, M.A.,** Abdel-Aziz, H.A., Allam, H.A. "Design, synthesis, in vitro, and in vivo evaluation of novel phthalazinone-based derivatives as promising acetylcholinesterase inhibitors for treatment of Alzheimer's disease." Drug Development Research, (**2023**) 84(6), pp. 1231–1246. DOI: 10.1002/ddr.22082	3.8	0

Abstract

Twenty novel phthalazinone-based compounds were designed as acetylcholinesterase (hAChE) inhibitors. Compounds 7e and 17c demonstrated comparable or superior activity compared to donepezil, respectively, in in vitro enzyme assay. Moreover, both compounds 7e and 17c possess minimal toxicity on hepatic and neuroblastoma cell lines. Besides, it was proved that compounds 7e and 17c have percentage alternations and a transfer latency time comparable to donepezil and can alleviate the cognitive impairment caused by the scopolamine-induced model in mice. The kinetic analysis for compound 17c suggested this compound as a mixed-type inhibitor that could bind to both the peripheral (PAS) and the catalytic site (CAS) of the hAChE enzyme. The synthesized molecules were subjected to in silico analyses, including molecular docking studies, and the outcomes were consistent with the in vitro findings.

No.	Publication	IF	Citations
11.	Ezzat, M.A.F., Elmasry, G.F., El-Mageed, M.M.A.A., **Fouad, Marwa A.,** Abdel-Aziz, H.A., Elewa, S.I. "Design, synthesis, and biological evaluation of furan-bearing pyrazolo[3,4-b]pyridines as novel inhibitors of CDK2 and P53–MDM2 protein–protein interaction." Drug Development Research, (**2023**) 84(6), pp. 1183–1203. DOI: 10.1002/ddr.22079	3.8	0

Abstract

The novel series of furan-bearing pyrazolo[3,4-b]pyridines were designed as cyclin-dependent kinase 2 (CDK2) inhibitors and as p53-murine double minute 2 (MDM2) inhibitors. The newly synthesized compounds were screened for their antiproliferative activity toward hepatocellular carcinoma (HepG2) and breast cancer (MCF7) cell lines. The most active compounds on both cell lines were additionally evaluated for their in vitro CDK2 inhibitory activity. Compounds 7b and 12f displayed enhanced activity (half-maximal inhibitory concentration [IC50] = 0.46 and 0.27 µM, respectively) in comparison to the standard roscovitine (IC50 = 1.41 ± 0.03 µM), in addition to, cell cycle arrest at S phase and G1/S transition phase in MCF7 cells treated with both compounds, respectively. Moreover, the most active spiro-oxindole derivative against MCF7 cell line, 16a, exhibited enhanced inhibitory activity against p53-MDM2 interaction in vitro (IC50 = 3.09 ± 0.12 µM) compared to nutlin, and increased the levels of both p53 and p21 by nearly fourfold in comparison to the negative control. Molecular docking studies demonstrated the plausible interaction patterns of the most potent derivatives 17b and 12f in the CDK2 binding pocket and the spiro-oxindole 16a with p53-MDM2 complex, respectively. Consequently, the new chemotypes 7b, 12f, and 16a can be presented as promising antitumor hits for further studies and optimization.

No.	Publication	IF	Citations
12.	Ahmed, R.F., Mahmoud, W.R., Abdelgawad, N.M., **Fouad, M.A.,** Said, M.F. "Exploring novel anticancer pyrazole benzenesulfonamides featuring tail approach strategy as carbonic anhydrase inhibitors." European Journal of Medicinal Chemistry, (**2023**) 261, 115805. DOI: 10.1016/j.ejmech.2023.115805	6.7	0

Abstract

This study aimed to design potent carbonic anhydrase inhibitors (CAIs) based on pyrazole benzenesulfonamide core. Nine series of substituted pyrazole benzenesulfonamide compounds were synthesized with variable groups like sulphamoyl group as in compounds 4a-e, its bioisosteric carboxylic acid as in compounds 5a-e and 8e, ethyl carboxylate ester as in compounds 6a-e and 9a-e, which were designed as potential prodrugs, isothiazole ring as in compound 7, hydrazide derivative 10e, hydroxamic acid derivatives 11a-e and semicarbazide derivatives 12a-c,e. All the synthesized compounds were investigated for their carbonic anhydrase (CA) inhibitory activity against two human CA isoforms hCA IX and hCA XII and compared to acetazolamide (AAZ). Also, the compounds were assessed for their anticancer activity against 60 cancer cell lines according to the US NCI protocol. Compounds 4b, 5b, 5d, 5e, 6b, 9b, 9e and 11b revealed significant inhibitory activity against both isoforms hCA IX and hCA XII, while 6e, 9d, 11d and 11e showed significant inhibitory activity against hCA XII only compared to acetazolamide as a reference. This would highlight these compounds as promising anticancer drugs. Moreover, compound 6e revealed a remarkable cytostatic activity against CNS cancer cell line (SF-539; TGI = 5.58 µM), renal cancer cell line (786-0; TGI = 4.32 µM) and breast cancer cell line (HS 578 T; TGI = 5.43 µM). Accordingly, compound 6e was subjected to cell cycle analysis and apoptotic assay on the abovementioned cell lines at the specified GI50 (0.45, 0.89 and 1.18 µM, respectively). Also, it revealed the increment of total apoptotic cells percentage in 786-0 (53.19%), SF-539 (46.11%) and HS 578 T (43.55%) relative to the control cells (2.07, 2.64 and 2.52%, respectively). In silico prediction of BBB permeability showed that most of the calculations for compound 6e resulted as BBB (+), which is required for a compound targeting CNS. Further, the interaction of the most active compounds with the key amino acids in the active sites of hCA IX and hCA XII was highlighted by molecular docking analysis.

No.	Publication	IF	Citations
13.	Ehab Elkady, **Marwa Fouad**, Ayoub Mozayad. "Application of Box–Behnken Design and Response Surface Methodology for Selecting the Optimum RP-HPLC Conditions for the Simultaneous Determination of Paracetamol and Diclofenac Sodium Along With Three Skeletal Muscle Relaxants in Three Different Pharmaceutical Dosage Forms." Journal of chromatographic science, (**2023**) In press. DOI: 10.1016/j.ejmech.2023.115805	1.3	2

Abstract

This study aimed to design potent carbonic anhydrase inhibitors (CAIs) based on pyrazole benzenesulfonamide core. Nine series of substituted pyrazole benzenesulfonamide compounds were synthesized with variable groups like sulphamoyl group as in compounds 4a-e, its bioisosteric carboxylic acid as in compounds 5a-e and 8e, ethyl carboxylate ester as in compounds 6a-e and 9a-e, which were designed as potential prodrugs, isothiazole ring as in compound 7, hydrazide derivative 10e, hydroxamic acid derivatives 11a-e and semicarbazide derivatives 12a-c,e. All the synthesized compounds were investigated for their carbonic anhydrase (CA) inhibitory activity against two human CA isoforms hCA IX and hCA XII and compared to acetazolamide (AAZ). Also, the compounds were assessed for their anticancer activity against 60 cancer cell lines according to the US NCI protocol. Compounds 4b, 5b, 5d, 5e, 6b, 9b, 9e and 11b revealed significant inhibitory activity against both isoforms hCA IX and hCA XII, while 6e, 9d, 11d and 11e showed significant inhibitory activity against hCA XII only compared to acetazolamide as a reference. This would highlight these compounds as promising anticancer drugs. Moreover, compound 6e revealed a remarkable cytostatic activity against CNS cancer cell line (SF-539; TGI = 5.58 µM), renal cancer cell line (786-0; TGI = 4.32 µM) and breast cancer cell line (HS 578 T; TGI = 5.43 µM). Accordingly, compound 6e was subjected to cell cycle analysis and apoptotic assay on the abovementioned cell lines at the specified GI50 (0.45, 0.89 and 1.18 µM, respectively). Also, it revealed the increment of total apoptotic cells percentage in 786-0 (53.19%), SF-539 (46.11%) and HS 578 T (43.55%) relative to the control cells (2.07, 2.64 and 2.52%, respectively). In silico prediction of BBB permeability showed that most of the calculations for compound 6e resulted as BBB (+), which is required for a compound targeting CNS. Further, the interaction of the most active compounds with the key amino acids in the active sites of hCA IX and hCA XII was highlighted by molecular docking analysis.

No.	Publication	IF	Citations
14.	Sandy N Aziz , Alia A Badawy , Demiana I Nessem , **Nevine S Abd El Malak** , Marianne J Naguib. "Chitosan-coated alginate (CCA) nanoparticles for augmentation of topical antihistaminic activity of diphenhydramine: in-vitro optimization, skin histopathology and pharmacodynamic studies with in vitro/in vivo correlation." Drug development &industrial pharmacy. (**2023**) Apr;49(4):316-327. DOI: 10.1080/03639045.2023.2211672	3.4	0

Abstract

Objective: The aim of the present study was to formulate chitosan-coated alginate nanoparticles containing the drug diphenhydramine hydrochloride (DHH).

Significance: Diphenhydramine hydrochloride (DHH) is the prototype of H1-antihistaminic drugs. It is a lipophilic drug, that easily crosses the blood-brain barrier when taken orally causing decrements in alertness and performance. Multiple applications of topical drug products are required. Thus, drug incorporation in nanocarriers would increase the skin penetration powers increasing the drug efficacy.

Methods: Chitosan-coated alginate (CCA) nanoparticles were prepared via polyelectrolyte complex technique adopting 23 full factorial designs. Three factors, namely, alginate concentration, drug-to-alginate ratio and CaCl2 volume, each in two levels were studied. The prepared formulae were evaluated utilizing entrapment efficiency (EE), particle size (PS), polydispersity index (PDI), zeta potential (ZP) and in vitro release. The characterization process was then followed by optimization.

Results: At alginate conc. of 1%, drug to alginate ratio of 2:1 and CaCl2 volume of 4 mL, NP8 was chosen as a candidate formula. Histopathological examination on shaved rat dorsal skin disclosed the safety of NP8 with no signs of necrosis or even inflammation. The enhanced topical delivery of diphenhydramine hydrochloride enclosed in the developed nanoparticles was further proved by induction of allergic reaction using intradermal histamine injection. The results revealed the superior ability of NP8 to decrease the diameter of the formed wheal in comparison to the marketed DHH product.
Conclusion: Thus, CCA nanoparticles are considered candidate nanocarriers for fortifying the topical antihistaminic activity of DHH.

No.	Publication	IF	Citations
15.	Reham Hammad, Rania Sanad, **Nevine S. Abd El Malak**, Randa Latif. "Cubosomal-functionalized block copolymer platform for dual delivery of linagliptin and empagliflozin: Recent advances in synergistic strategies for maximizing control of high-risk type II diabetes." Drug Delivery and Translational Research. (**2023**). DOI: 10.1080/03639045.2023.2211672	5.4	0

Abstract

A well-made chitosan-PVP block copolymer platform was equipped with highly ordered and uniform nano-channels. This highly adhesive block copolymer platform was designed to ensure the efficient co-delivery of two synergistic-acting hypoglycemic drugs. Linagliptin oral bioavailability is 30% due to poor permeability and intestinal degradation. Its pharmacokinetics shows a non-linear profile. Empagliflozin exhibited decreased permeability and decreased solubility in aqueous media between pH 1 and 7.5. Cubosomes were functionalized as a good microdomain to guest and improve the physicochemical characteristics of drug molecules with decreased permeability and solubility. Cubosomes loaded with linagliptin (linagliptin cubosomes (LCs)) and empagliflozin (empagliflozin cubosomes ECs) were separately prepared using the top-down method and optimized by applying 23 factorial design. Optimized cubosomal systems LCs (F3) and ECs (F4) were incorporated into a chitosan-PVP gel to obtain dual cubosome-loaded platforms (LECF) optimized through 22 factorial design. The permeation study from the optimized LECF (C1) ensured enhanced empagliflozin permeation alongside continued efflux for linagliptin, resolving potential risks due to its non-linear plasma profile. The in-vivo study revealed that AUC(0-∞) of linagliptin and empagliflozin was enhanced by 2- and threefold, respectively. Therefore, the chitosan-PVP block copolymer platform buccal application for the co-delivery of linagliptin and empagliflozin could contribute to enhanced clinical effectiveness in treating diabetes. Graphical abstract showing dual cubosome-loaded platform tested in-vivo using a rabbit model.

No.	Publication	IF	Citations
16.	**Fahim SA**, Ibrahim S, Tadros SA, Badary OA. "Protective effects of butylated hydroxytoluene on the initiation of N-nitrosodiethylamine-induced hepatocellular carcinoma in albino rats." Hum Exp Toxicol. (**2023**) DOI: 10.1177/09603271231165664	2.8	1

Abstract

diethylenetriamine (DEN), a hepatocarcinogen, is found in a variety of smoked and fried foods and was reported to be hepatotoxic in mice. Butylated hydroxytoluene (BHT) is a potent antioxidant used in cosmetic formulations and as a food additive and preservative. As a result, BHT was studied as a potential inhibitor in the early stages of diethylnitrosamine (DEN)-induced HCC. Male Wistar albino rats (n = 24) were equally subdivided. Group 1 was the negative control; Group 2 and 3 administered BHT and DEN, respectively; Group 4 received BHT followed by DEN. Blood samples and rat livers were taken for biochemical and histological investigation. Hepatotoxicity was assessed by increased liver enzymes and HCC indicators, along with reduced antioxidant and pro-apoptotic factors. AFP, AFPL3, GPC3, GSH, SOD, MDA, CASP3 and BAX expression increased significantly after DEN treatment. DEN also reduced GPx, CAT, and CYP2E1 activity, and BCl-2 expression. Moreover, in the hepatic parenchyma, the DEN caused histological alterations. Pretreatment with BHT enhanced antioxidant status while preventing histopathological and most biochemical alterations. BHT pretreatment suppresses DEN-initiated HCC by decreasing oxidative stress, triggering intrinsic mitotic apoptosis, and preventing histopathological changes in liver tissue.

No.	Publication	IF	Citations
17.	Badr AM, Elkholy O, Said M, **Fahim SA**, El-Khatib M, Sabry D, Gaber RM. "Diagnostic significance of hsa_circ_0000146 and hsa_circ_0000072 biomarkers for Diabetic Kidney Disease in patients with type 2 diabetes mellitus." J Med Biochem. (**2023**) Mar 15;42(2):239-248. DOI: 10.5937/jomb0-39361	2.5	0

Abstract

Background: Diabetic Kidney Disease (DKD) is a significant challenge in healthcare. However, there are currently no reliable biomarkers for renal impairment diagnosis, prognosis, or staging in DKD patients. CircRNAs and microRNAs have emerged as noninvasive and efficient biomarkers.

Methods: We explored Cannabinoid receptor 1 (CNR1), C reactive protein (CRP), hsa_circ_0000146 and 0000072, and hsa-miR-21 and 495 as diagnostic biomarkers in DKD. The serum concentrations of CRP and CNR1 were measured using ELISA. Rt-qPCR was used to evaluate the expression levels of CNR1, circRNAs, and miRNAs in 55 controls, 55 type 2 diabetes mellitus patients, and 55 DKD patients. Their diagnostic value was determined by their ROC curve. KEGG pathway was used to predict the functional mechanism of the circRNA's target genes.

Results: DKD patients exhibited a significant increase in CRP and CNR1 levels and the expression of miR-21 and 495. The expression levels of circ_0000146 and 0000072 decreased in DKD patients. ROC analysis revealed that circRNAs and miRNAs alone or CNR1 and CRP have significant diagnostic potential. The functional prediction results showed the involvement of hsa_circ_0000146 and 0000072 in various pathways that regulate DKD.

Conclusions: Therefore, the examined circRNAs and miRNAs may represent a novel noninvasive biomarker for diagnosing and staging DKD.

No.	Publication	IF	Citations
18.	ElMonier AA, El-Boghdady NA, **Fahim SA**, Sabry D, Elsetohy KA, Shaheen AA. "LncRNA NEAT1 and MALAT1 are involved in polycystic ovary syndrome pathogenesis by functioning as competing endogenous RNAs to control the expression of PCOS-related target genes." Noncoding RNA Res. (**2023**) Mar 3;8(2):263-271. DOI: 10.1016/j.ncrna.2023.02.008	5	2

Abstract

Accumulating evidence has shown an abnormal expression of several non-coding RNAs in ovarian tissues which might be closely linked with the pathogenesis of PCOS. The aim of this study was to identify competing endogenous (ce) RNA network: long non-coding RNA (lncRNA), microRNA (miRNA) and their target genes: androgen receptor (AR), follistatin (FST) and insulin receptor substrate-2 (IRS-2), which are relevant to PCOS, to underline the molecular pathogenesis of PCOS and assist in early diagnosis and treatment. Bioinformatic analysis was performed to retrieve a ceRNA network: [lncRNA (NEAT1 and MALAT1) - miRNA (miR-30a-5p and miR-30d-5p) - mRNA (AR, FST and IRS-2)] linked to PCOS. Expression of the selected RNAs was examined by qPCR in peripheral blood leukocytes obtained from 73 PCOS patients (41 obese and 32 non-obese) and 31 healthy controls. PCOS patients showed significantly higher expression levels of NEAT1, miR-30a-5p, AR, FST and IRS-2, with significantly lower expression levels of MALAT1 and miR-30d-5p relative to controls especially in obese versus non-obese patients. Receiver operating characteristic (ROC) curve analysis indicated that most of the selected RNAs could serve as potential early diagnostic markers for PCOS with the highest efficiency obtained upon combining NEAT1 and miR-30d-5p or MALAT1 and miR-30a-5p with either of PCOS target genes. Moreover, all addressed RNAs had been proved as potential predictors of PCOS. The obtained data of ceRNA network raised the possibility that NEAT1 overexpression may increase the expression levels of AR, FST and IRS-2 by sponging miR-30d-5p, while low expression of MALAT1 may allow higher expression of the above genes via increasing miR-30a-5p, suggesting their involvement in PCOS pathogenesis and promising role for future diagnosis and targeted therapy.

No.	Publication	IF	Citations
19.	Shimaa Abdelsattar, **Sally A. Fahim**, Hiba S Al-Amodi, Hala F.M. Kamel, Zeinab A. Kasemy, Fatma O. Khalil, Mahmoud S. Abdallah, Hanan M Bedair, Abd El-Naser Abd El-Ati Gad Alla, Alyaa Sabry, Mohamed A. Sakr, Mahmoud Selim, Eman M. Abd Elgayed. "The Potential Role of Circulating Long miscellaneous RNAs in the Diagnosis and Prognosis of hepatitis C related Hepatocellular Carcinoma". Non-Coding RNA. (**2023**) DOI: doi.org/10.3390/ncrna9050062	4.5	0

Abstract

Ribonucleic acids (RNAs) are important regulators of gene expression and crucial for the progression of hepatocellular carcinoma (HCC). This study was designed to determine the diagnostic and prognostic utility of the circulating long miscellaneous RNAs; LINC01419, AK021443, and AF070632 in HCV-related HCC patients. Real-time PCR was used to measure their relative expression levels in the plasma of 194 HCV patients, 120 HCV-related HCC patients and 120 healthy controls. LINC01419 and AK021443 expression levels had significantly increasing linear trend estimates while AF070632 was dramatically downregulated in HCC compared to HCV. Interestingly, LINC01419 and AK021443 served as more significant diagnostic biomarkers for HCC than AF070632 and AFP. Multivariate analysis with cox regression revealed that the high expression of AK021443 [HR = 10.06, CI95%: 3.36–30.07], the high expression of LINC01419 [HR 4.13, CI95%: 1.32–12.86], and the low expression of AF070632 [HR = 2.70, CI95%: 1.07–6.81] were significant potential prognostic factors for HCC. Besides, the Kaplan–Meier analysis showed that HCC patients with high LIN01419 and AK021443 and low AF070632 expression levels had shorter OS. The circulating LINC01419 and AK021443 can be used as noninvasive potential biomarkers for diagnosis and prognosis of HCV-related HCC patients than AF070632 providing new targets for limiting the progression of the disease.

No.	Publication	IF	Citations
20.	**Ewaisha, R.,** & Anderson, K. S. "Immunogenicity of CRISPR therapeutics—Critical considerations for clinical translation." Frontiers in Bioengineering and Biotechnology. (**2023**), volume 11. DOI: 10.3389/fbioe.2023.1138596	5.7	5

Abstract

CRISPR offers new hope for many patients and promises to transform the way we think of future therapies. Ensuring safety of CRISPR therapeutics is a top priority for clinical translation and specific recommendations have been recently released by the FDA. Rapid progress in the preclinical and clinical development of CRISPR therapeutics leverages years of experience with gene therapy successes and failures. Adverse events due to immunogenicity have been a major setback that has impacted the field of gene therapy. As several in vivo CRISPR clinical trials make progress, the challenge of immunogenicity remains a significant roadblock to the clinical availability and utility of CRISPR therapeutics. In this review, we examine what is currently known about the immunogenicity of CRISPR therapeutics and discuss several considerations to mitigate immunogenicity for the design of safe and clinically translatable CRISPR therapeutics.

No.	Publication	IF	Citations
21.	Mariam Omara, Mohamed Hagras, Mohamed M Elsebaie, Nader S Abutaleb, Hanzada T Nour El-Din, Maria O Mekhail, Ahmed S Attia, Mohamed N Seleem, Marwa T Sarg, Abdelrahman S Mayhoub. "Exploring novel aryl/heteroaryl-isosteres of phenylthiazole against multidrug-resistant bacteria." RSC Adv. (2023) Jul 6;13(29):19695-19709. DOI: 10.1039/d3ra02778c	3.9	1

Abstract

Antimicrobial resistance has become a concern as a worldwide threat. A novel scaffold of phenylthiazoles was recently evaluated against multidrug-resistant Staphylococci to control the emergence and spread of antimicrobial resistance, showing good results. Several structural modifications are needed based on the structure-activity relationships (SARs) of this new antibiotic class. Previous studies revealed the existence of two key structural features essential for the antibacterial activity, the guanidine head and lipophilic tail. In this study, a new series of twenty-three phenylthiazole derivatives were synthesized utilizing the Suzuki coupling reaction to explore the lipophilic part. The in vitro antibacterial activity was evaluated against a range of clinical isolates. The three most promising compounds, 7d, 15d and 17d, with potent MIC values against MRSA USA300 were selected for further antimicrobial evaluation. The tested compounds exhibited potent results against the tested MSSA, MRSA, and VRSA strains (concentration: 0.5 to 4 μg mL-1). Compound 15d inhibited MRSA USA400 at a concentration of 0.5 μg mL-1 (one-fold more potent than vancomycin) and showed low MIC values against ten clinical isolates, including linezolid-resistant strain MRSA NRS119 and three vancomycin-resistant isolates VRSA 9/10/12. Moreover, compound 15d retained its potent antibacterial activity using the in vivo model by the burden reduction of MRSA USA300 in skin-infected mice. The tested compounds also showed good toxicity profiles and were found to be highly tolerable to Caco-2 cells at concentrations of up to 16 μg mL-1, with 100% of the cells remaining viable.

No.	Publication	IF	Citations
22.	El-Din, H.T.N.; Elsebaie, M.M.; Abutaleb, N.S.; Kotb, A.M.; **Attia, A.S.**; Seleem, M.N.; Mayhoub, A.S. "Expanding the structure–activity relationships of alkynyl diphenylurea scaffold as promising antibacterial agents." RSC Medicinal Chemistry (**2023**), 14, 367-377. DOI: 10.1039/d2md00351a	4.1	1

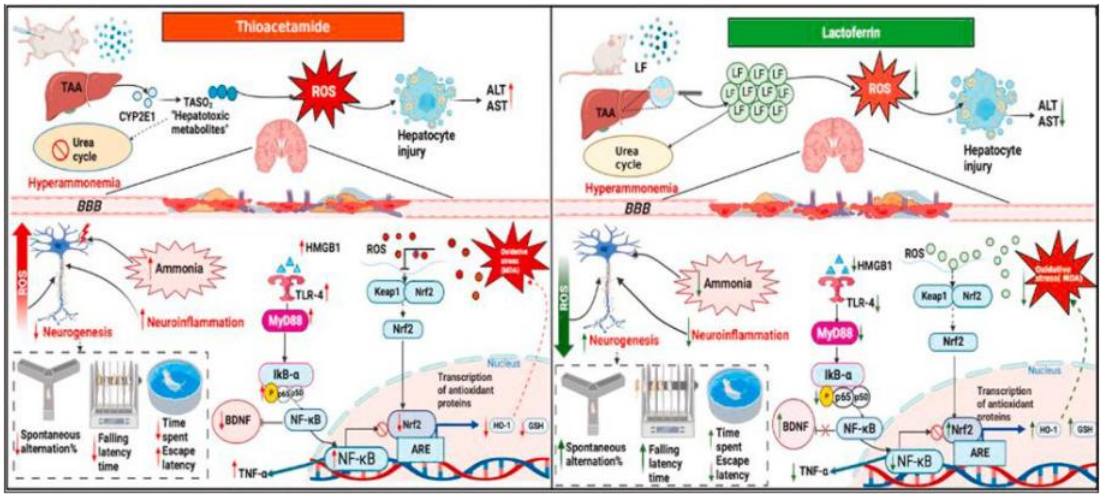
Abstract

With the continuous and alarming threat of exhausting the current antimicrobial arsenals, efforts are urgently needed to develop new effective ones. In this study, the antibacterial efficacy of a set of structurally related acetylenic-diphenylurea derivatives carrying the aminoguanidine moiety was tested against a panel of multidrug-resistant Gram-positive clinical isolates. Compound 18 was identified with a superior bacteriological profile than the lead compound I. Compound 18 demonstrated an excellent antibacterial profile in vitro: low MIC values, extended post-antibiotic effect, refractory ability to resistance development upon extended repeated exposure, and high tolerability towards mammalian cells. Finally, when assessed in a MRSA skin infection animal model, compound 18 showed considerable healing and less inflammation, decrease in the bacterial loads in skin lesions, and it surpassed fusidic acid in controlling the systemic dissemination of S. aureus. Collectively, compound 18 represents a promising lead anti-MRSA agent that merits further investigation for the development of new anti-staphylococcal therapeutics.

No.	Publication	IF	Citations
23.	Essam, R.M., Saadawy, M.A., Gamal, M., Abdelsalam, R.M., El-Sahar, A.E. „Lactoferrin averts neurological and behavioral impairments of thioacetamide-induced hepatic encephalopathy in rats via modulating HGMB1/TLR-4/MyD88/Nrf2 pathway.“ Neuropharmacology, (2023), 236, 109575. DOI: 10.1016/j.neuropharm.2023.109575	4.7	0

Abstract

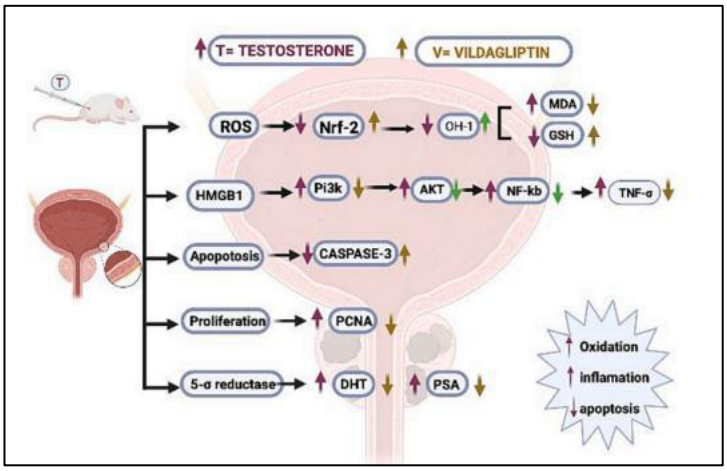
Hepatic encephalopathy (HE) is a life-threatening disease caused by acute or chronic liver failure manifested by aberrant CNS changes. In the present study, we aimed to explore the neuroprotective effect of lactoferrin (LF) against thioacetamide (TAA)-induced HE in rats. Animals were divided into four groups, control, LF control, TAA-induced HE, and LF treatment, where LF was administered (300 mg/kg, p.o.) for 15 days in groups 2 and 4 meanwhile, TAA (200 mg/kg, i.p.) was given as two injections on days 13 and 15 for the 3rd and 4th groups. Pretreatment with LF significantly improved liver function observed as a marked decline in serum AST, ALT, and ammonia, together with lowering brain ammonia and enhancing motor coordination as well as cognitive performance. Restoration of brain oxidative status was also noted in the LF-treated group, where lipid peroxidation was hampered, and antioxidant parameters, Nrf2, HO-1, and GSH, were increased. Additionally, LF downregulated HMGB1, TLR-4, MyD88, and NF-κB signaling pathways, together with reducing inflammatory cytokine, TNF-α, and enhancing brain BDNF levels. Moreover, the histopathology of brain and liver tissues revealed that LF alleviated TAA-induced liver and brain deficits. In conclusion, the promising results of LF in attenuating HMGB1/TLR-4/MyD88 signaling highlight its neuroprotective role against HE associated with acute liver injury via ameliorating neuroinflammation, oxidative stress, and stimulating neurogenesis.



No.	Publication	IF	Citations
24.	**El-Sahar, A.E., Bekhit, N., Eissa, N.M., Abdelsalam, R.M., Essam, R.M.** "Targeting HMGB1/PI3K/Akt and NF-κB/Nrf-2 signaling pathways by vildagliptin mitigates testosterone-induced benign prostate hyperplasia in rats." Life Sciences, (**2023**), 322, 121645 DOI: 10.1016/j.lfs.2023.121645	6.1	2

Abstract

Benign prostatic hyperplasia (BPH) is a prevalent illness in older adults. It is well-recognized that testosterone is essential in the onset of BPH. Vildagliptin (Vilda), a dipeptidyl peptidase-IV inhibitor, has been shown to have anti-inflammatory and antioxidant effects. In this study, we studied the effects of vildagliptin on testosterone-induced BPH in rats and its underlying mechanisms. Forty male Wistar rats were allocated into four groups (n = 10): CTRL, Vilda, BPH, and BPH + Vilda groups. Our results revealed that vildagliptin treatment considerably lessened the prostate weight, prostate index, serum levels of prostate-specific antigen, 5α-reductase activity, and DHT levels compared to the testosterone group. Furthermore, vildagliptin treatment inhibited the expression of HMGB1, PI3K/Akt/NF-κB, and TNF-α signaling pathways in the prostate tissue of diseased rats. Additionally, vildagliptin treatment increased the expression of Nrf-2 and HO-1, reduced GSH levels, and lowered MDA levels. Besides, vildagliptin noticeably scaled up the level of cleaved caspase-3 enzyme and, conversely, the protein expression of proliferating cell nuclear antigen (PCNA). Correspondingly, vildagliptin counteracts testosterone-induced histological irregularities in rats' prostates. These findings suggest that vildagliptin may be a potential prophylactic approach to avoid BPH.



No.	Publication	IF	Citations
25.	Abdalhameid, E., Abd El-Haleim, E.A., **Abdelsalam, R.M.,** Fawzy, H.M., Kenawy, S.A. "Cinnamic acid mitigates methotrexate-induced lung fibrosis in rats: comparative study with pirfenidone." Naunyn-Schmiedeberg's Archives of Pharmacology, (**2023**). DOI: 10.1007/s00210-023-02652-w	3.6	0

Abstract

Purpose: Lung fibrosis is a heterogeneous lung condition characterized by excessive accumulation of scarred tissue, leading to lung architecture destruction and restricted ventilation. The current work was conducted to examine the probable shielding influence of cinnamic acid against lung fibrosis induced by methotrexate.

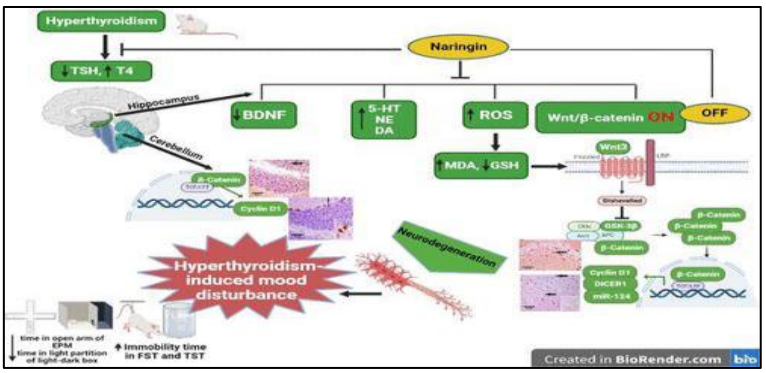
Methods: Rats were pre-treated with oral administration of cinnamic acid (50 mg/kg/day) for 14 days, whereas methotrexate (14 mg/kg) was orally given on the 5th and 12th days of the experiment. Pirfenidone (50 mg/kg/day) was used as a standard drug. At the end of the experiment, oxidative parameters (malondialdehyde, myeloperoxidase, nitric oxide, and total glutathione) and inflammatory mediators (tumor necrosis factor-α and interleukin-8), as well as transforming growth factor-β and collagen content, as fibrosis indicators, were measured in lung tissue.

Results: Our results revealed that cinnamic acid, as pirfenidone, effectively prevented the methotrexate-induced overt histopathological damage. This was associated with parallel improvements in oxidative, inflammatory, and fibrotic parameters measured. The outcomes of cinnamic acid administration were more or less the same as those of pirfenidone. In conclusion, pre-treatment with cinnamic acid protects against methotrexate-induced fbrosis, making it a promising prophylactic adjuvant therapy to methotrexate and protecting against its possible induction of lung fibrosis.

No.	Publication	IF	Citations
26.	Mai A Abd-Elmawla, Reham M Essam, Kawkab A Ahmed, Maha Abdelmonem. "Implication of Wnt/GSK-3β/β-Catenin Signaling in the Pathogenesis of Mood Disturbances Associated with Hyperthyroidism in Rats: Potential Therapeutic Effect of Naringin." ACS Chem Neurosci. (2023);14(11):2035-2048. DOI: 10.1021/acschemneuro.3c00013.	5	4

Abstract

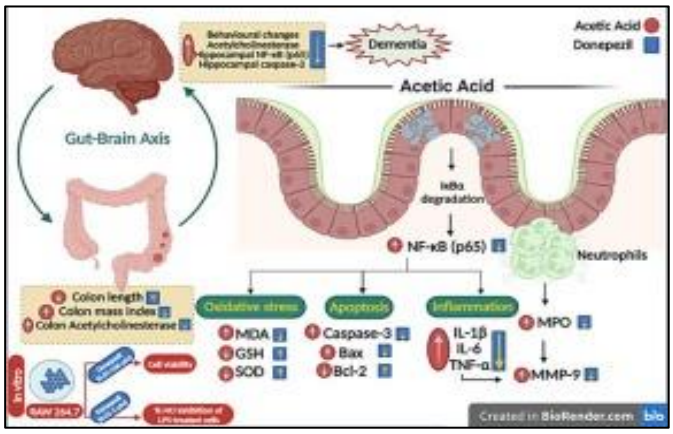
Patients with hyperthyroidism are commonly diagnosed with mood disorders. Naringin, (4',5,7-trihydrocyflavanone-7-O-rhamnoglucoside), a natural bioflavonoid, has many neurobehavioral activities including anxiolytic and antidepressant properties. The role of Wingless (Wnt) signaling in psychiatric disorders is considered substantial but debatable. Recently, regulation of Wnt signaling by naringin has been reported in different disorders. Therefore, the present study aimed to investigate the possible role of Wnt/GSK-3β/β-catenin signaling in hyperthyroidism-induced mood disturbances and explore the therapeutic effects of naringin. Hyperthyroidism was induced in rats by intraperitoneal injection of 0.3 mg/kg levothyroxine for 2 weeks. Naringin was orally administered to rats with hyperthyroidism at a dose of 50 or 100 mg/kg for 2 weeks. Hyperthyroidism induced mood alterations as revealed by behavioral tests and histopathological changes including marked necrosis and vacuolation of neurons in the hippocampus and cerebellum. Intriguingly, hyperthyroidism activated Wnt/p-GSK-3β/β-catenin/DICER1/miR-124 signaling pathway in the hippocampus along with an elevation in serotonin, dopamine, and noradrenaline contents and a reduction in brain-derived neurotrophic factor (BDNF) content. Additionally, hyperthyroidism induced upregulation of cyclin D-1 expression, malondialdehyde (MDA) elevation, and glutathione (GSH) reduction. Naringin treatment alleviated behavioral and histopathological alterations and reversed hyperthyroidism-induced biochemical changes. In conclusion, this study revealed, for the first time, that hyperthyroidism could affect mental status by stimulating Wnt/p-GSK-3β/β-catenin signaling in the hippocampus. The observed beneficial effects of naringin could be attributed to increasing hippocampal BDNF, controlling the expression of Wnt/p-GSK-3β/β-catenin signaling as well as its antioxidant properties.



No.	Publication	IF	Citations
27.	Eman M Elbaz, Reham M Essam, Kawkab A Ahmed, Maheera H Safwat. "Donepezil halts acetic acid-induced experimental colitis in rats and its associated cognitive impairment through regulating inflammatory/oxidative/apoptotic cascades: An add-on to its anti-dementia activity." Int Immunopharmacol. (2023), 116:109841. DOI: 10.1016/j.intimp.2023.109841	5.6	4

Abstract

Ulcerative colitis (UC) is a persistent inflammatory bowel disease (IBD) that is regarded as a risk factor for cognitive impairment. Donepezil (DON), a centrally acting acetylcholinesterase inhibitor (AChEI), is approved for the management of Alzheimer's disease (AD). We aimed to scrutinize the impact of DON on acetic acid (AA)-induced UC in rats and to evaluate its ability to attenuate inflammatory response, oxidative strain, and apoptosis in this model and its associated cognitive deficits. Rats were categorized into: normal, DON, AA, and AA + DON groups. DON (5 mg/kg/day) was administered orally for 14 days either alone or beginning with the day of UC induction. Colitis was evoked by a single transrectal injection of 1 ml of 4 % acetic acid. Results revealed that DON significantly improved the behavioral abnormalities with the mitigation of inflammation, apoptosis, and histopathological changes in the hippocampi of the colitis group. Moreover, DON significantly alleviated the macroscopic and microscopic changes associated with colitis. Interestingly, DON inhibited pro-inflammatory cytokines via suppression of AA-induced activation of nuclear factor kappa-B (NF-κB), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β) in the colon, along with serum IL-1β. DON inhibited colon lipid peroxidation, restored the antioxidants with a significant amelioration of the degree of neutrophil infiltration, and repressed colitis-induced matrix metalloproteinases-9 (MMP-9) production. Furthermore, DON decreased the Bax/Bcl-2 ratio and caspase-3 protein expressions. Eventually, in lipopolysaccharide (LPS)-treated RAW 264.7 macrophage cells, DON suppressed nitric oxide (NO) release, demonstrating the ability of DON to significantly curtail inflammation in immune cells. Taken together, DON ameliorated experimental colitis and its linked cognitive dysfunction, possibly via its antioxidant effect and modulation of pro-inflammatory cytokines and apoptosis. Thereby, DON could be a therapeutic nominee for UC and associated neurological disorders.



No.	Publication	IF	Citations
28.	**Reham M Essam**, Esraa A Kandil. "p-CREB and p-DARPP-32 orchestrating the modulatory role of cAMP/PKA signaling pathway enhanced by Roflumilast in rotenone-induced Parkinson's disease in rats." Chem Biol Interact. (**2023**) 25:372:110366. DOI: 10.1016/j.cbi.2023.110366.	5.1	1

Abstract

Recently, phosphodiesterases (PDEs) have gained great attention due to their implication in Parkinson's disease (PD) pathogenesis. Noteworthy, the PDE4 enzyme is highly expressed in the striatum and selectively degrades cyclic adenosine monophosphate (cAMP). The cAMP was shown to play a vital role in dopamine (DA) signaling besides maintaining the plasticity of dopaminergic neurons as well as protecting them from inflammation and oxidative stress-mediated death. Thus, PDE4 inhibition could be a promising strategy for treating PD. Accordingly, the present study investigated the neuroprotective efficacy of roflumilast, a PDE4 inhibitor, in abolishing neurodegeneration in the rotenone-induced PD model. Rotenone (1.5 mg/kg, s.c) was delivered via 11 injections on matching days. Roflumilast treatment (0.5 mg/kg, p.o) was given daily after the fifth rotenone injection. Roflumilast significantly reversed rotenone's adverse effects, as it enhanced trophic factors expression and abrogated inflammation as well as oxidative stress. Thus, promoting dopaminergic neuronal plasticity and survival, as well as restoring striatal DA level and function, which resulted in enhanced motor performance. The beneficial effect of roflumilast was mediated through inhibition of striatal PDE4 with consequent activation of cAMP-dependent protein kinase A (PKA) signaling pathways, including the cAMP response element-binding protein (CREB) pathway and dopamine and cAMP-regulated phosphoprotein 32,000 (DARPP-32) pathway that is essential for maintaining dopaminergic function. Therefore, the present work sheds light on the substantial neuroprotective potential of roflumilast in treating PD through the activation of the cAMP/PKA cascade.

No.	Publication	IF	Citations
29.	Mona M Saber, Manal Moustafa Mahmoud, Hesham M Amin, **Reham M Essam**. "Therapeutic effects of combining curcumin and swimming in osteoarthritis using a rat model." Biomed Pharmacother. (**2023**) 166:115309. DOI: 10.1016/j.biopha.2023.115309	7.5	0

Abstract

Osteoarthritis (OA) is a common debilitating degenerative disease of the elderly. We aimed to study the therapeutic effects of combining curcumin and swimming in monosodium iodoacetate (MIA)-induced OA in a rat model. The rats were divided into 5 groups (n = 9). Group 1 received saline and served as a control group. Groups 2–5 were injected intra-articularly in the right knee with 100 µL MIA. One week later, groups 3 and 5 were started on daily swimming sessions that gradually increased to 20-mins per session, and for groups 4 and 5, oral curcumin was administered at a dose of 200 mg/kg for 4 weeks. The combination therapy (curcumin + swimming) showed the most effective results in alleviating pain and joint stiffness as well as improving histological and radiological osteoarthritis manifestations in the knee joints. The combination modality also reduced serum C-reactive protein and tissue cartilage oligomeric matrix protein levels. Mechanistically, rats received dual treatment exhibited restoration of miR-130a and HDAC3 expression. The dual treatment also upregulated PPAR-γ alongside downregulation of NF-κB and its inflammatory cytokine targets TNF-α and IL-1β. Additionally, there was downregulation of MMP1 and MMP13 in the treated rats. In conclusion, our data showed that there is a therapeutic potential for combining curcumin with swimming in OA, which is attributed, at least in part, to the modulation of miR-130a/HDAC3/PPAR-γ signaling axis.

No.	Publication	IF	Citations
30.	Shohda A El-Maraghy, Aya Reda, **Reham M Essam**, Mona A Kortam. "The citrus flavonoid "Nobiletin" impedes STZ-induced Alzheimer's disease in a mouse model through regulating autophagy mastered by SIRT1/FoxO3a mechanism." Inflammopharmacology (**2023**);31(5):2701-2717. DOI: 10.1007/s10787-023-01292-z.	5.8	0

Abstract

The prominence of autophagy in the modulation of neurodegenerative disorders has sparked interest to investigate its stimulation in Alzheimer's disease (AD). Nobiletin possesses several bioactivities such as anti-inflammation, antioxidation, and neuroprotection. Consequently, the study's aim was to inspect the possible neurotherapeutic impact of Nobiletin in damping AD through autophagy regulation. Mice were randomly assigned into: Group I which received DMSO, Groups II, III, and IV obtained STZ (3 mg/kg) intracerebroventricularly once with Nobiletin (50 mg/kg/day; i.p.) in Group III and Nobiletin with EX-527 (2 mg/kg, i.p.) in Group IV. Interestingly, Nobiletin ameliorated STZ-induced AD through enhancing the motor performance and repressing memory defects. Moreover, Nobiletin de-escalated hippocampal acetylcholinesterase (AChE) activity and enhanced acetylcholine level while halting BACE1 and amyloid-β levels. Meanwhile, Nobiletin stimulated the autophagy process through activating the SIRT1/FoxO3a, LC3B-II, and ATG7 pathway. Additionally, Nobiletin inhibited Akt pathway and controlled the level of NF-κB and TNF-α. Nobiletin amended the oxidative stress through enhancing GSH and cutting down MDA levels. However, EX527, SIRT1 inhibitor, counteracted the neurotherapeutic effects of Nobiletin. Therefore, the present study provides a strong verification for the therapeutic influence of Nobiletin in AD. This outcome may be assigned to autophagy stimulation through SIRT1/FoxO3a, inhibiting AChE activity, reducing neuroinflammation and oxidative stress.

No.	Publication	IF	Citations
31.	Hanan H. Ahmed, **Reham M. Essam**, Muhammed F. El-Yamany, Kawkab A. Ahmed and **Ayman E. El-Sahar**. "Unleashing lactoferrin's antidepressant potential through the PI3K/Akt/mTOR pathway in chronic restraint stress rats." Food Function (**2023**). DOI: 10.1039/d3fo02222f.	6.1	0

Abstract

Depression is a widespread neuropsychiatric illness whose etiology is yet mysterious. Lactoferrin (LF), an iron-binding glycoprotein, is reported to promote neuroprotection through its role in the modulation of oxidative stress and inflammation. The objective of the present research was to evaluate the efficacy of LF against chronic restraint stress (CRS)-induced depressive behavior in rats. Depression was evidenced by a reduced grooming time in the splash test and an increased immobility time in the tail suspension test (TST) and forced swimming test (FST). This effect was also accompanied by reduced GSH and serotonin levels and elevated lipid peroxidation and corticosterone levels in the hippocampus. Additionally, an exaggerated hippocampal inflammatory response was also shown by a rise in NF-κB (p65) and TNF-α levels and a reduced IL-10 level. Moreover, CRS substantially reduced the BDNF content as well as the protein levels of PI3K, Akt, and mTOR while boosting the GSK3β content. Interestingly, LF therapy significantly improved CRS-induced behavioral and biochemical aberrations, an effect which was suppressed upon pretreatment with LY294002 (PI3K inhibitor). This suggests that the antidepressant potential of LF may be mediated through the modulation of the PI3K/Akt/mTOR signaling pathway. Furthermore, LF succeeded in restoring 5-HT and corticosterone levels, diminishing oxidative stress and ameliorating the inflammatory cascades. Therefore, and for the first time, LF might serve as a promising antidepressant drug through targeting the PI3K/Akt/mTOR pathway.

No.	Publication	IF	Citations
32.	Hebatollah E Eitah, Hanan Naeim Attia, Ahmed A F Soliman, Amina A Gamal El Din, Khaled Mahmoud, Rabab H Sayed, Yousreya A Maklad, **Ayman E El-Sahar**. "Vitamin D ameliorates diethylnitrosamine-induced liver preneoplasia: A pivotal role of CYP3A4/CYP2E1 via DPP-4 enzyme inhibition." Toxicology and Applied Pharmacology (**2023**) 1:458:116324. DOI: 10.1016/j.taap.2022.116324.	**3.8**	**0**

Abstract

Growing evidence has indicated that vitamin D (Vit D) regulates cell proliferation and differentiation in cancer cells. Accordingly, the present study was conducted to investigate the possible beneficial effects of Vit D on diethylnitrosamine (DEN)-induced liver preneoplasia. The effect of Vit D on HepG2 cells was investigated using MTT assay. Additionally, liver preneoplasia was induced in Swiss male albino mice by giving overnight fasted animals 5 consecutive doses of DEN (75 mg/kg/week). Oral treatment with Vit D (200 IU/kg/day) was initiated either 2 weeks before DEN (first protocol) or 1 week after the first dose of DEN injection (second protocol). At the end of the experiment, tissue levels of GGT, DPP-4, TNF-α, IL-6, CYP2E1, and CYP3A4 were also estimated. Moreover, the histopathological study of liver tissue and immunohistochemical detection of GST-P, PCNA, and NF-κB were performed. Vit D exerted a significant cytotoxic effect on HepG2 cells via significantly increasing BAX, p53, and BAX/Bcl2 ratio, and significantly decreasing Bcl2 mRNA expression. In both in vivo protocols, Vit D was capable of normalizing relative liver weight, PCNA, altered hepatocellular foci, and ductular proliferation. Moreover, Vit D significantly reduced the DEN-induced elevation of AST, ALT, ALP, GGT, DDP-4, TNF-α, IL-6, CYP2E1, liver DNA damage, GST-P, NF-κB, nuclear hyperchromatic/pleomorphism, cholestasis, and inflammatory cell aggregates, but significantly increased CYP3A4 content. In conclusion, current results reflect the potential impact of Vit D in the management of early stages of liver cancer.