Publications Template

#	Research Title	Field	Abstract	Year of Publication Publishing	Publishing Link "URL"
1	Cross-relationship between COVID-19 infection and anti-obesity products efficacy and incidence of side effects: A cross-sectional study	Pharmacology & Pharmacy	**Background** Obesity and COVID-19 are at the top of nowadays health concerns with significant crosstalk between each other. The COVID-19 pandemic negatively affected healthy lifestyles and increased obesity prevalence. Thus, there was a surge in anti-obesity products (AOPs) intake. Herein, we evaluated how the pandemic has affected slimming products' efficacy and safety in patients seeking weight reduction at an urban, weight management centre in Alexandria, Egypt. In addition, the effect of AOPs on COVID-19 infection severity was also appraised to	2024	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0309323

			detect whether AOPs can alter COVID-19 host cell entry and infective mechanisms, and thus, affect infection severity. **Methods** Patients were invited to complete an anonymous survey. The survey assessed self-reported changes in weight, the use of AOPs during the COVID-19 pandemic, COVID-19 infection severity, AOPs efficacy, and incidence of side effects. Inclusion criteria were obese patients above 18 years old who got infected by COVID-19 while receiving a single-ingredient AOP. **Results** A total of 462 participants completed our anonymous validated questionnaire. Most of the participants were females (450; 98.4%) with BMI ranging from 24.98–58.46. Eligible participants were only 234 and the top-administered products were orlistat, liraglutide, metformin,		

			green tea, cinnamon, *Garcinia cambogia*, and *Gymnema Sylvestre*. In most cases, AOPs intake was beneficial for COVID-19 infection, and most patients experienced mild-to-moderate COVID-19 symptoms. On the other hand, SARS-CoV-2 significantly interferes with AOPs' mechanisms of action which positively or negatively influences their efficacy and side effects incidence due to predictable pharmacological link. **Conclusion** Concurrent AOPs intake with COVID-19 infection is a two-sided weapon; AOPs attenuate COVID-19 infection, while SARS-CoV-2 interferes with efficacy and side effects incidence of AOPs.		
2	Valsartan as a prophylactic treatment against	Pharmacology & Pharmacy	Aims Transactivation of insulin-growth-factor-receptor (IGF-1R) by angiotensin-II-type-1-receptor (AT-1R) was only	2024	https://www.sciencedirect.com/science/article/abs/pii/S0024320524005290

	breast cancer development and niche activation: What molecular sequels follow chronic AT-1R blockade?		demonstrated in vascular-smooth-muscle cells and has never been tested in breast-cancer (BC). This investigation addressed the impact of chronic AT-1R blockade by valsartan (Val) on possible concurrent AT-1R/IGF-1R signaling inhibition, regressing BC-tumor-microenvironment (TME) cellular components activation, and hindering BC development. Main methods The effect of different Val doses (10, 20, 40 & 80 mg/kg/day for 490 days) was tested on dimethylbenz(*a*)anthracene (DMBA)-induced progesterone-promoted-BC in rats. The influence on intratumoral/circulating angiotensin-II (ANG-II) levels and AT-1R/Mas-R immunofluorescent-expression were assessed. The potential AT-1R/IGF-1R crosstalk within TME-BC-stem-cells		

			(BCSCs) and cancer-associated-fibroblasts (CAFs) was evaluated by fluorescently marking these cells and locating the immunofluorescently-stained AT-1R/IGF-1R in them using confocal-laser-microscopy and further quantified by flow cytometry. In addition, the molecular alterations following blocking AT-1R were inspected including determining Src; crucial for IGF-1R transactivation by AT-1R, Notch-1; IGF-IR transcriptional-regulator, and PI3K/Akt &IL-6/STAT expression. Further, the suppression of CSCs' capabilities to maintain pluripotency, stemness features, epithelial-to-mesenchymal-transition (EMT), and angiogenesis was evaluated by assessing NANOG gene, aldehyde-dehydrogenase (ALDH), N-cadherin and vascular-endothelial-growth-factor		

			(VEGF), respectively. Furthermore, the proliferative marker; Ki-67, was detected by immunostaining, and tumors were histologically graded using Elston-Ellis-modified-Scarff-Bloom-Richardson method. Key findings Prophylactic Val significantly reduced tumor size, prolonged latency, reduced tumor histopathologic grade, decreased circulating/intratumoral-ANG-II levels, increased Mas-R, and decreased AT1R expression. AT-1R/IGF-1R were co-expressed with a high correlation coefficient on CAFs/BCSCs. Moreover, Val significantly attenuated IGF-1R transactivation and transcriptional regulation via Src and Notch-1 genes' downregulation and reduced Src/IGF-IR-associated PI3K/Akt and IL-6/STAT3 signaling. Further, Val significantly decreased		

			intratumoral NANOG, ALDH, N-cadherin, VEGF, and Ki-67 levels. Significance Chronic Val administration carries a potential for repurposing as adjuvant or conjunct therapy for patients at high risk for BC.		
3	Metabolomic insights into the therapeutic mechanisms of costus (Saussurea costus (Falc.) Lipsch.) root extract in propylthiouracil-induced hypothyroidism rat model	Pharmacology & Pharmacy	Ethnopharmacological relevance Saussurea costus (Falc.) Lipschitz. is one of the most reputed medicinal plants as a traditional medicine in the Arab and Middle East regions in the treatment of thyroid disorders, however, more investigations are needed to fully understand its effectiveness and mechanism of action. Aim of the study The primary objective of the study was to assess the impact of *Saussurea costus* (COST) on the metabolic profiles of propylthiouracil (PTU)-induced hypothyroidism in	2024	https://www.sciencedirect.com/science/article/abs/pii/S0378874124000837

			rats. This involves a comprehensive examination of serum metabolites using UPLC/QqQ-MS analysis aiming to identify differential metabolites, elucidate underlying mechanisms, and evaluate the potential pharmacological effect of COST in restoring metabolic homeostasis. Materials and methods Hypothyroidism was induced in female Sprague-Dawley rats by oral administration of propylthiouracil (PTU). UPLC/QqQ MS analysis of serum samples from normal, PTU, and PTU + COST rats was utilized for annotation of intrinsic metabolites with the aid of online Human metabolome database (HMDB) and extensive literature surfing. Multivariate statistical analyses, including orthogonal partial least squares discriminant analysis (OPLS-DA), discerned variations between the		

			different groups. Serum levels of T3, T4 and TSH in addition to arachidonic acid (ARA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) levels in thyroid gland tissues; Phospholipase A2 group IIA (PLA2G2A), and lipoprotein lipase (LPL) in liver tissues were assessed by specific ELISA kits. Gene expression for key proteins of the primary evolved pathwayswere quantified by one-step qRT-PCR technique. Histopathological evaluation of thyroid gland tissue was performed by an investigator blinded to the experimental group using light microscope. Results Distinct clustering in multivariate statistical analysis models indicated significant variations in serum chemical profiles among normal, disease, and treated groups. VIP values guided the selection of differential		

			metabolites, revealing significant changes in metabolite concentrations. Subsequent to COST treatment, 43 differential intrinsic metabolites exhibited a notable tendency to revert towards normal levels. Annotated metabolites, such as lysophosphatidylcholine (L PC), L-acetylcarnitine, gamma-glutamylserine, and others, showed differential regulation in response to PTU and subsequent *S. costus* treatment. Notably, 21 metabolites were associated with polyunsaturated fatty acids (PUFAs) biosynthesis, arachidonic acid (ARA) metabolism, and glycerophospholipid meta bolism exhibited significant changes on conducting metabolic pathway analysis. Conclusions COST improves PTU-induced hypothyroidism by regulating biosynthesis of PUFAs signified by n-3/n-6, ARA		

			and glycerophospholipid meta bolism. The study provides us a novel mechanism to explain the improvement of hypothyroidism and associated dyslipidemia by COST, depicts a metabolic profile of hypothyroidism, and gives us another point cut for further exploring the biomarkers and pathogenesis of hypothyroidism.		
4	Reactive astrocytes targeting with oral vitamin A: Efficient neuronal regeneration for Parkinson's disease treatment and reversal of associated liver fibrosis	Pharmacology & Pharmacy	Introduction A recent approach to cure neurodegenerative diseases is to reprogram fibroblasts into functioning neurons using multiple exogenous transcription factors (TFs) and micro-RNAs. Administering agents that can endogenously induce these TFs may bypass the limitations of this approach. Astrocytes may represent a part of the extrahepatic-stellate system involved in vitamin-A (V_A) homeostasis. Activated-stellate cells lose their V_A-	2023	https://onlinelibrary.wiley.com/doi/full/10.1111/cns.14179

			storage capacity, and this was previously applied for hepatic-stellate cells (HSCs) targeting to treat liver fibrosis. Accordingly, it is hypothesized that Parkinson's disease (PD) may be coupled with retinoid depletion that may extract V_A from V_A-rich-HSCs triggering liver fibrosis. Thus, V_A administration may selectively target V_A-deficient reactive astrocytes and HSCs. Besides, V_A has the regenerative capability and may induce endogenous-TFs generation. Methods Fluorescently labeled V_A-coupled liposomes (FLV) were traced using confocal laser microscope in rats with induced PD for detecting brain accumulation and uptake into fluorescently labeled astrocytes. Liver fibrosis associated with PD was assessed biochemically and histopathologically, while V_A deficiency was confirmed		

			by assessing retinol-binding protein gene expression in the brain and liver. Multiple V_A doses were tested for reversing PD-associated liver fibrosis, generating TFs (involved in reprograming astrocytes/fibroblasts into different neuronal types) and capability of dopaminergic-neurons regeneration. Results Fluorescently labeled V_A-coupled liposomes revealed selective brain accumulation and uptake into astrocytes. PD was associated with significant liver fibrosis and V_A deficiency in the brain and liver. Furthermore, V_A-medium dose (VAMD) was the optimum one for reversing PD-associated liver fibrosis, generating multiple astrocytes/fibroblasts reprogramming TFs, regenerating dopaminergic neurons, and improving PD. Conclusion		

			V_A-medium dose pursued brain targeting in PD with the potential capability of regenerating neurons and restoring dopaminergic transmission. This may place this therapy as an essential treatment in PD management protocol.		
5	Nicorandil reduces morphine withdrawal symptoms, potentiates morphine antinociception, and ameliorates liver fibrosis in rats	Pharmacology & Pharmacy	Aims Chronic liver disease (CLD) is a serious medical condition affecting patients globally and pain management poses a unique challenge. ATP-sensitive potassium channels (K_{ATP}) are expressed in nociceptive neurons and hepatic cells. We tested the hypothesis whether morphine and nicorandil, K_{ATP} channel opener, alone and in combination possess hepatoprotective, antinociceptive effect and alter morphine physical dependence. Main methods	2023	https://www.sciencedirect.com/science/article/abs/pii/S002432052300156X

			Intraperitoneal injection (i.p.) of carbon tetrachloride (CCl_4) induced liver fibrosis in male Wistar rats. Nicorandil (15 mg/kg/day) was administered per os for two weeks. Morphine (3.8, 5, 10 mg/kg, i.p.) was administered prior to antinociception testing in tail flick and formalin tests. Morphine physical dependence following naloxone injection, fibrotic, oxidative stress markers, and liver histopathology were assessed. Key findings Morphine alone, produced insignificant changes of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), hyaluronic acid (HA), hepatic hydroxyproline (Hyp), malondialdehyde (MDA), and superoxide dismutase (SOD) levels and exerted significant antinociception in		

			the pain models. Nicorandil alone protected against liver damage (decreased serum ALT, AST, HA, hepatic Hyp, MDA, increased SOD levels, improved fibrosis scores). Nicorandil/morphine combination produced remarkable hepatoprotection a nd persistent analgesia compared to morphine alone as evidenced by reduced (EC50) of morphine. Nicorandil augmented morphine analgesia and markedly decreased withdrawal signs in morphine-dependent rats. Significance The data showed for the first time, the hepatoprotection and augmented antinociception mediated by nicorandil/morphine combination in liver fibrosis via antioxidant and antifibrotic mechanisms. Nicorandil ameliorated withdrawal signs in morphine dependence in CLD. Thus,		

			combining nicorandil/morphine provides a novel treatment strategy to ameliorate hepatic injury, potentiate antinociception and overcome morphine-induced physical dependence in liver fibrosis.		
6	Novel celecoxib-loaded chitosan-fucoidan nanoparticles as potential immunotherapy for oral squamous cell carcinoma: Mechanistic insights	Pharmacology & Pharmacy	Celecoxib (CXB), a selective COX-2 inhibitor, is a component of triple-oral-metronomic-chemotherapy. However, chronic CXB utilization in high doses could bring about major cardiovascular consequences. The CXB incorporation into chitosan (CS)/fucoidan (FCD) nanoparticles (NPs) could be expected to reduce drug toxicity, improve epithelial drug permeation, and enhance drug delivery to COX-2 over-expressing sites within TME. CXB-loaded CS/FCD NPs were developed and evaluated for particle size, zeta potential, entrapment efficiency, morphology, and *in*	2023	https://www.sciencedirect.com/science/article/abs/pii/S1773224723000801

			vitro drug release. SCC-4 cells were used to test the cytotoxic, antiproliferative, and pro-apoptotic effects by performing MTT, Ki-67, and Annexin-V assays, respectively. The selective uptake of CS/FCD NPs by labelled tumor immune cells (TICs), tumor-endothelial-cells (TECs), and myeloid-derived-suppressor-cells (MDSCs) was determined qualitatively and quantitatively. Furthermore, signaling molecules, including Jagged-1/Notch-signaling, and biomarkers of TICs, TECs, and MDSCs; such as TGF-β, IL-6, aldehyde dehydrogenase, and arginase-1/iNOS, were analyzed in harvested SCC-4 cells pre-treated with CXB-CS/FCD-NPs, plain FCD and CXB. The best achieved CXB-CS1FCD5 NPs were spherical in shape, and possessed an optimum size (226.4 nm), promising zeta potential (−26.30 mV), high		

			entrapment efficiency (76.78%), and allowed sustained CXB release. They showed the utmost anti-proliferative, pro-apoptotic and cell-cycle arrest in SCC-4 cells with greater accumulation within MDSCs. Neither FCD nor CXB in their plain form could affect all of the tested TME cellular biomarkers. On contrary, CXB-CS/FCD NPs had significantly affected all of the investigated biomarkers. This study highlighted the synergistic antitumor potential of CXB-CS/FCD NPs against oral cancer, at lower CXB doses, and provided some mechanistic insights that can in part explain the observed anticancer efficacy.		
7	Fucoidan/hyaluronic acid cross-linked zein nanoparticles loaded with fisetin	Pharmacology & Pharmacy	Fisetin (FS) is an anticancer drug having potential role in oral tumors management. However, its clinical application is limited due to its hydrophobicity and instability. Bioactive	2023	https://www.sciencedirect.com/science/article/abs/pii/S0141813023014228

	as a novel targeted nanotherapy for oral cancer		polymers-based nanosystems have a great potential in cancer therapy. Herein, different biopolymers were selected for their anticancer activity and targeting ability for nanoparticles preparation namely; fucoidan (FU), zein (Zn) and hyaluronic acid (HA). The selected FS-loaded cross-linked Zn nanoparticles (ZFH) which contains HA& FU for Zn nanoparticles stabilization showed the most suitable particle size (196 ± 6.53 nm), mean surface net charge (−38.8 ± 1.47 mV) and entrapment efficiency (98 ± 1.2 %). This is the first study to utilize both HA &FU not only for stabilization but also for dual targeting effect due to their targeting ability to multiple tumor targets. *In-vitro* anticancer activity of ZHF revealed remarkable uptake by SCC-4 cells with significant cytotoxic action. Further, ZHF was appraised using 4-nitroquinoline 1-oxide		

			(4-NQO)-induced oral cancer *in-vivo*; ZHF significantly reduced OSCC-specific serum biomarkers levels, histologic tumor grade and increased caspase-3 level. Moreover, potential of destroying two key tumor regulatory cells; TECs and CSCs, was evaluated using their specific markers. The elaborated ZFH nanoparticles could be considered as promising targeted nanotherapy for oral cancer treatment with enhanced efficacy and survival rate.		
8	Nicorandil/ morphine crosstalk accounts for antinociception and hepatoprotection in hepatic fibrosis in rats: Distinct	Pharmacology & Pharmacy	Previous report indicated that nicorandil potentiated morphine antinociception and attenuated hepatic injury in liver fibrotic rats. Herein, the underlying mechanisms of nicorandil/morphine interaction were investigated using pharmacological, biochemical, histopathological, and molecular docking studies. Male Wistar rats were injected	2023	https://www.sciencedirect.com/science/article/pii/S0753332223008594

	roles of opioid/cGMP and NO/KATP pathways		intraperitoneally (i.p.) with carbon tetrachloride (CCl_4, 40%, 2 ml/kg) twice weekly for 5 weeks to induce hepatic fibrosis. Nicorandil (15 mg/kg/day) was administered per os (p.o.) for 14 days in presence of the blockers; glibenclamide (K_{ATP} channel blocker, 5 mg/kg, p.o.), L-N^G-nitro-arginine methyl ester (L-NAME, nitric oxide synthase inhibitor, 15 mg/kg, p.o.), methylene blue (MB, guanylyl cyclase inhibitor, 2 mg/kg, i.p.) and naltrexone (opioid antagonist, 20 mg/kg, i.p.). At the end of the 5th week, analgesia was evaluated using tail flick and formalin tests along with biochemical determinations of liver function tests, oxidative stress markers and histopathological examination of liver tissues. Naltrexone and MB inhibited the antinociceptive activity of		

			the combination. Furthermore, combined nicorandil/morphine regimen attenuated the release of endogenous peptides. Docking studies revealed a possible interaction of nicorandil on μ, κ and δ opioid receptors. Nicorandil/morphine combination protected against liver damage as evident by decreased liver enzymes, liver index, hyaluronic acid, lipid peroxidation, fibrotic insults, and increased superoxide dismutase activity. Nicorandil/morphine hepatoprotection and antioxidant activity were inhibited by glibenclamide and L-NAME but not by naltrexone or MB. These findings implicate opioid activation/cGMP versus NO/K_{ATP} channels in the augmented antinociception, and hepatoprotection, respectively, of the combined therapy and implicate provoked cross talk by nicorandil and morphine on		

			opioid receptors and cGMP signaling pathway. That said, nicorandil/morphine combination provides a potential multitargeted therapy to alleviate pain and preserve liver function. Graphical Abstract		
9	Novel mucoadhesive celecoxib-loaded cubosomal sponges: Anticancer potential and regulation of myeloid-derived suppressor cells in oral squamous cell carcinoma	Pharmacology & Pharmacy	Oral squamous-cell carcinoma (OSCC) is a widespread health problem. Myeloid-derived suppressor cells (MDSCs) are major tumor microenvironment (TME) population that govern many carcinogenesis aspects by establishing immunosuppressive milieu favoring tumor aggressiveness and treatment resistance. Cyclooxygenase-2 (COX-2) regulates MDSCs activity, hence, COX-2-selective inhibition by celecoxib (CXB) showed good anticancer effect at relatively high doses with possible subsequent cardiovascular complications. Therefore, targeted CXB	2023	https://www.sciencedirect.com/science/article/abs/pii/S0939641122002934

			delivery to MDSCs may represent a promising OSCC treatment strategy. Novel mucoadhesive-cubosomal buccal sponges were prepared for MDSCs targeting and were evaluated for their *in-vitro* quality attributes, *ex-vivo* mucoadhesion using buccal chicken-mucosa. Optimally-selected formulation showed considerable uptake by $CD33^{+}/11b^{+}$MDSCs in human OSCC cell-line (SCC-4) when quantitatively analyzed by flow-cytometry and examined using confocal-laser microscope. Optimum formulations loaded with low CXB doses (12 mg) were promoted to *in-vivo* studies via local application, using 4-nitroquinoline-1-oxide-induced OSCC in rats, and compared to their corresponding CXB gels. SP16 revealed the highest ability to decrease MDSC activation, recruitment and		

			TME-immunosuppression in the isolated tumors. Consequently, SP16 exerted the greatest capacity to reduce histologic tumor grade, the OSCC-specific serum tumor markers levels, cancer hallmarks and stemness markers. CXB-loaded cubosomal sponges preferentially target MDSCs with noticeable anticancer potential and may exemplify novel mucoadhesive nanocarriers for OSCC treatment.		
10	Reversal of fibrosis and portal hypertension by Empagliflozin treatment of CCl_4-induced liver fibrosis: Emphasis on gal-	Pharmacology & Pharmacy	To date, liver fibrosis has no clinically approved treatment. Empagliflozin (EMPA), a highly selective sodium-glucose-cotransporter-2 (SGLT2) inhibitor, has shown ameliorative potential in liver diseases without revealing its full mechanisms. Neuropilin-1 (NRP-1) is a novel regulator of profibrogenic signaling pathways related to hepatic stellate cells (HSCs) and	2023	https://www.sciencedirect.com/science/article/abs/pii/S0014299923005782

	1/NRP-1/TGF-β and gal-1/NRP-1/VEGFR2 pathways		hepatic sinusoidal endothelial cells (HSECs) that modulates intrahepatic profibrogenic and angiogenic pathways. Herein, EMPA's antifibrotic potentials and effects on galactin-1 (Gal-1)/NRP-1 signaling pathways have been evaluated in an experimental liver fibrosis rat model by testing different EMPA dose regimens. EMPA treatment brought a dose-dependent decrease in Gal-1/NRP-1 hepatic expression. This was coupled with suppression of major HSCs pro-fibrotic pathways; transforming growth factor-β (TGF-β)/TGF-βRI/Smad2 and platelet-derived growth factor-beta (PDGF-β) with a diminution of hepatic Col 1A1 level. In addition, EMPA prompted a protuberant suppression of the angiogenic pathway; vascular endothelial growth factor (VEGF)/VEGF-receptor-2 (VEGFR-2)/SH2-Domain Containing Adaptor Protein-B		

			(Shb), and reversal of altered portal hypertension (PHT) markers; endothelin-1 (ET-1) and endothelial nitric oxide synthase (eNOS). The amelioration of liver fibrosis was coupled with a remarkable improvement in liver aminotransferases and histologic hepatic fibrosis Ishak scores. The highest EMPA dose showed a good safety profile with minimal changes in renal function and glycemic control. Thus, the current study brought about novel findings for a potential liver fibrosis treatment modality via targeting NRP-1 signaling pathways by EMPA.		
11	Unraveling putative antiulcer phytoconstituents against *Helicobacter pylori* urease and	Pharmacology & Pharmacy	Globally peptic ulcer disease is a severe public health issue caused by an imbalance between the defensive and aggressive mechanisms. In the current study, the phytochemical components of various organs (leaf, fruit, seed, and bark) of *Jacaranda*	2023	https://www.sciencedirect.com/science/article/abs/pii/S0026265X23001686

	human H^+/K^+-ATPase from *Jacaranda mimosifolia* using UPLC-MS/MS coupled to chemometrics and molecular docking		*mimosifolia D. Don* collected from Egypt at different seasons and geographical locations were investigated. UPLC-MS/MS allows a tentative identification of 53 compounds where flavonoids, quinoids, and triterpenoids represented the major identified classes. Multivariate statistical analysis (principle component analysis (PCA), hierarchical cluster analysis (HCA)-heat map and orthogonal projection to latent structures-discriminate analysis (OPLS-DA), and accompanied coefficient plots) was applied to investigate in-between and within-class discrimination of the different organs of *Jacaranda mimosifolia D. Don*. The obtained extracts were tested for their inhibitory activities against *Helicobacter pylori* Urease and human H^+/K^+-ATPase enzymes. Fruit extract showed the highest inhibitory activity against *H.*		

			pylori urease. Meanwhile, leaf extract was found to be more potent, against human H^+/K^+-ATPase. The results of the biological activities were further modeled using Partial Least Squares Regression (PLSR) analysis together with the quantitative data. The optimal number of latent variables was determined with the aid of Variables important for the projection (VIP) plot to remove the uninformative variables. The developed model was validated using root mean square error of calibration (RMSEC), cross-validation (RMSECV) and prediction (RMSEP). PLS model coefficient plots showed that flavonoids as isoquercitrin and rutin were the most contributing metabolites/biomarkers to the detected anti-urease and H^+/K^+-ATPase activities, respectively. Molecular docking analysis was utilized to gain more insights into the		

			interaction modalities for the top fifteen metabolites obtained from the PLS model with the active sites of urease and H^+/K^+-ATPase enzymes. In agreement with the model coefficients, isoquercitrin and rutin were ranked as the top hits for the studied enzymes. To validate the results, in vitro inhibitory assays were performed on isoquercitrin and rutin. Potent inhibitory activities were determined against urease and H^+/K^+-ATPase with IC50 ± SD of 9.10 ± 0.75 µM and 0.61 ± 0.06 µM for isoquercitrin and rutin, respectively.		
12	Alleviation of liver cirrhosis and associated portal-hypertension by *Astragalus* species	Pharmacology & Pharmacy	Liver cirrhosis is a late-stage liver disease characterized by excessive fibrous deposition triggering portal-hypertension (PH); the prime restrainer for cirrhosis-related complications. Remedies that can dually oppose hepatic fibrosis and lower PH, may prevent progression into	2022	https://www.nature.com/articles/s41598-022-15958-1

	in relation to their UPLC-MS/MS metabolic profiles: a mechanistic study		decompensated-cirrhosis. Different *Astragalus*-species members have shown antifibrotic and diuretic actions with possible subsequent PH reduction. However, *A.spinosus and A.trigonus* were poorly tested for eliciting these actions. Herein, *A.spinosus* and *A.trigonus* roots and aerial parts extracts were subjected to comprehensive metabolic-fingerprinting using UHPLC-MS/MS resulting in 56 identified phytoconstituents, followed by chemometric untargeted analysis that revealed variable metabolic profiles exemplified by different species and organ types. Consequently, tested extracts were *in-vivo* evaluated for potential antifibrotic/anticirrhotic activity by assessing specific markers. The mechanistic prospective to induce diuresis was investigated by analyzing plasma aldosterone and renal-		

			transporters gene-expression. Serum apelin and dimethylarginine-dimethylaminohydrolase-1 were measured to indicate the overall effect on PH. All extracts amended cirrhosis and PH to varying extents and induced diuresis via different mechanisms. Further, An OPLS model was built to generate a comprehensive metabolic-profiling of *A.spinosus* and *A.trigonus* s econdary-metabolites providing a chemical-based evidence for their efficacious consistency. In conclusion, *A.spinosus* and *A.t rigonus* organs comprised myriad pharmacologically-active constituents that act synergistically to ameliorate cirrhosis and associated PH.		
13	Biologically-guided isolation of natural lead antithyroid drug from	Pharmacology & Pharmacy	Hyperthyroidism is a common endocrine disorder associated with increased risk of cardiovascular complications and mortality. Although antithyroid drugs (ATDs) are	2020	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9261795/

	Medicago sativa L. sprouts and its toxic profile in comparison with propylthiouracil		approved as first line option for many hyperthyroidism cases, including pregnancy and childhood, they exert significant toxic profile. *Medicago sativa* L. (alfalfa) also called "The father of all food" was among the diet consumed by mares that gave birth to foals with congenital hypothyroidism. Since, greenfeed was accused for the development of such condition, alfalfa may possess constituents with promising antithyroid potential that could be a valuable substitute for the conventional ATDs. The current work was designed to identify the most biologically active antithyroid phytoconstituent separated from alfalfa sprouts and comparing its antithyroid mechanism, efficacy and toxic profile to the standard ATD; propylthiouracil (PTU). The most biologically active solvent fractions from alfalfa sprouts extract were identified		

			by *in vitro* screening for anti-thyroid peroxidase (TPO) activity, from which different phytoconstituents were separated and identified by interpretation of spectroscopic data. These compounds were then *in vitro* screened for anti-TPO and virtually screened via GLIDE XP docking into the crystal structures of the enzymes; bovine lactoperoxidase, as an alternative to TPO, and mammalian selenocysteine-dependent iodothyronine deiodinase (IDI), that are both uniquely dually prohibited by PTU. The compound that showed the least TPO IC_{50} and highest combined docking XP score was elected for comparing its antithyroid mechanism, efficacy, tendency to reverse hyperthyroidism-triggered complications and toxicity to PTU using L-thyroxine-induced hyperthyroidism model in rats. Seven compounds (1–7) were		

			isolated from the most biologically active fraction, whilst, compounds (4–7) were reported for the first time from alfalfa sprouts. Compound 5 (apigenin) showed the least TPO IC_{50} and highest *in-silico* combined score, thus, apigenin was selected for further *in-vivo* investigations. Apigenin was found to more effectively interfere with type 1-IDI than with TPO *in vivo*. Apigenin therapy resulted in nearly euthyroid state, without incidence of hypothyroidism, thyroid hypertrophy, hepatotoxity or WBCs count reduction. In addition, apigenin, but not PTU, corrected hyperthyroidism-induced left ventricular hypertyrophy. Therefore, apigenin is a natural lead antithyroid drug that represents a possible safer alternative to conventional ATDs.		
14	Vitamin B12 as a	Pharmacology	So far, the cholinergic hypothesis of Alzheimer's	2022	https://www.sciencedirect.com/science/article/pii/S0928098722000860

	cholinergic system modulator and blood brain barrier integrity restorer in Alzheimer's disease	& Pharmacy	disease (AD) remains the fundamental explanation for the complex etiopathology of AD. However, therapeutics raising synaptic acetylcholine (Ach) or having cholinergic receptors agonistic activity had shown limited clinical efficacy, possibly, due to lacking capability to aggregate cholinergic receptors within the degenerated cholinergic neurons. Vitamin-B12 (B12) is an epigenetic modifier. It has a specific CNS transport system via the cubam receptors. The later enclose a cholinergic aggregator; agrin protein, suggesting that B12 administration may cause cholinergic receptors aggregation. Further, B12 involvement in homocysteine (Hcy) metabolism may restore blood brain barrier (BBB) integrity disrupted by elevated Hcy levels in AD. Here in, using a pharmacological model of cholinergic amnesia, three		

			different B12 doses were compared to the standard of care; donepezil (DON) regarding cholinergic system modulation, and their effect on Hcy metabolic pathways. Further, AD-associated cerebro-vascular pathology was assessed by morphometric analyses of cerebro-vasculature morphology and ultrastructure using scanning and transmission electron-microscopes, respectively. Consequent effect on key AD-hallmarks and behavioral cognitive tests was also examined. The highest B12-tested dose (B12-HD) showed the greatest hippocampal cholinergic modulation with dose-dependent preferential upregulation of one cholinergic receptor over the other. Altered Hcy metabolism was proved to be a consequence of cholinergic disruption that was variably reversed by different B12 doses. In spite of equipotent		

			effect of DON and B12-HD therapies in decreasing β-amyloid synthesis, B12-HD-treated group revealed the greatest restoration of BBB integrity indicating superior capability of β-amyloid clearance. Therefore, B12-HD therapy may represent a promising AD-modifying agent with extra-ability over conventional cholinergic modulators to aggregate cholinergic receptors.		
15	Oral vitamin-A-coupled valsartan nanomedicine: High hepatic stellate cell receptors accessibility and prolonged enterohepatic residence	Pharmacology & Pharmacy	So far, liver fibrosis still has no clinically-approved treatment. The loss of stored vitamin-A (V_A) in hepatic stellate cells (HSCs), the main regulators to hepatic fibrosis, can be applied as a mechanism for their targeting. Valsartan is a good candidate for this approach; it is a marketed oral-therapy with inverse- and partial-agonistic activity to the over-expressed angiotensin-II type1 receptor (AT1R) and depleted nuclear peroxisome proliferator-activated receptor-	2018	https://www.sciencedirect.com/science/article/abs/pii/S0168365918302864

			gamma (PPAR-γ), respectively, in activated HSCs. However, efficacy on AT1R and PPAR-γ necessitates high drug permeability which is lacking in valsartan. In the current study, liposomes were used as nanocarriers for valsartan to improve its permeability and hence efficacy. They were coupled to V_A and characterized for HSCs-targeting. Tracing of orally-administered fluorescently-labeled V_A-coupled liposomes in normal rats and their fluorescence intensity quantification in different organs convincingly demonstrated their intestinal entrapment. On the other hands, their administration to rats with induced fibrosis revealed preferential hepatic, and less intestinal, accumulation which lasted up to six days. This indicated their uptake by intestinal stellate cells that		

			acted as a depot for their release over time. Confocal microscopical examination of immunofluorescently-stained HSCs in liver sections, with considerable formula accumulation, confirmed HSCs-targeting and nuclear uptake. Consequently, V_A-coupled valsartan-loaded liposomes (VLC)-therapy resulted in profound re-expression of hepatic Mas-receptor and PPAR-γ, potent reduction of fibrogenic mediators' level and nearly normal liver function tests. Therefore, VLC epitomizes a promising antifibrotic therapy with exceptional extended action and additional PPAR-γ agonistic activity.		
16	Hepatic stellate cell-targeted imatinib nanomedicine versus	Pharmacology & Pharmacy	Liver fibrosis is a global health problem without approved treatment. Imatinib inhibits two key profibrotic pathways; platelet-derived growth factor (PDGF) and transforming	2017	https://www.sciencedirect.com/science/article/abs/pii/S0168365917308696

	conventional imatinib: a novel strategy with potent efficacy in experimental liver fibrosis		growth factor-beta (TGF-β) and thus can be used to treat liver fibrosis. However, conventional imatinib therapy is hampered by low concentration at target tissue and increased toxicity to other tissues especially heart, lung and liver. Since hepatic stellate cells (HSCs) are the main contributors to liver fibrosis pathogenesis and sole hepatic vitamin A (V_A) storage cells, they can be actively targeted by coupling liposomes to V_A. In this study, novel V_A-coupled imatinib-loaded liposomes (ILC) were prepared and optimized regarding V_A-coupling efficiency, imatinib entrapment efficiency, and particle size. Preferential accumulation of the selected formula in liver was proved by tracing intraperitoneally (i.p.)-injected V_A-coupled liposomes loaded with Nile Red (LCNR) to rats with CCl_4-induced liver		

			fibrosis using live animal imaging. Co-localization of LCNR with immunofluorescently-labeled PDGFR-β in frozen liver tissue sections confirmed HSCs targeting. ILC bio-distribution, following single i.p. injection, revealed 13.5 folds higher hepatic accumulation than conventional imatinib in addition to limited bio-distribution to other organs including heart and lung reflecting diminished adverse effects. ILC therapy resulted in a potent inhibition of phosphorylated PDGFR-β expression when compared to conventional imatinib. Subsequently, there was a statistically significant improvement in liver function tests and reversal of hepatotoxicity along with liver fibrosis. Anti-fibrotic effect was evident from histopathologic Ishak score reduction as well as		

			normalization of the level of profibrotic mediators (hydroxyproline, TGF-B and matrix metalloproteinase-2). Thus, HSC-targeted imatinib therapy shows outstanding anti-fibrotic effects with reduced cytotoxicity compared to conventional imatinib. It can represent a promising novel approach for liver fibrosis treatment.		
17	Evaluation of the anticarcinogenic effect of some peroxisome proliferator activated receptor ligands on dimethylbenz (α) anthracene induced mammary tumor in female rats	Pharmacology & Pharmacy	Introduction: Breast cancer is the leading cause of cancer death among females worldwide. Peroxisome proliferator activated receptors (PPARs) are one of several nuclear receptors involved in the biology of breast cancer. Aim: Compare the effect of fenofibrate (PPARα ligand), pioglitazone (PPAR γ ligand) and omega-3 (PPARα, γ ligand) and their probable mechanisms of action on 7, 12 dimethylbenz (α) anthracene (DMBA)-induced mammary carcinoma in female rats.	2015	https://scholar.google.com.eg/citations?view_op=view_citation&hl=en&user=BjQdQEYAAAAJ&citation_for_view=BjQdQEYAAAAJ:UeHWp8X0CEIC

			Methods: Fifty female Waister albino rats were utilized, with ten serving as plain controls. The remaining were subjected to induction of mammary carcinomas by oral intubation with a single dose of 20 mg DMBA suspended in one ml of sesame oil. After the appearance of mammary tumors, rats were randomly assigned to 4 orally-treated groups: untreated, fenofibrate, pioglitazone and omega-3-treated for 28 days. Assessed parameters: Percentage change of tumor volume, serum and tumor tissue vascular endothelial growth factor levels, tumor caspase-3 and cyclooxygenase-2 concentrations, as well as immunohistochemical detection of Ki-67 expression. Results: The untreated rats had progressive increase in mammary tumor volume. Treatment with fenofibrate, pioglitazone or omega-3 significantly reduced the rate		

			of tumor growth via antiangiogenic, proapoptotic, antiproliferative and anti-inflammatory effects. Conclusion: Fenofibrate, pioglitazone and omega-3 exerted anti-tumor effects on breast cancer induced in rats via numerous mechanisms of action.		