Publications Template

#	Research Title	Field	Abstract	Year of Publication Publishing	Publishing Link "URL"
1	The Anti-inflammatory & Apoptotic effects of Atorvastatin in combination with Celecoxib in Adjuvant Induced Arthritis in rats). Journalof Pharmacy and Pharmacology. 2013; 3(4):58-66.	Drug repurposing In Rheumatoid arthritis (autoimmune disorder)	Statins seem to have anti-inflammatory effects independent of their lipid-lowering abilities. Previous studies demonstrated a strong synergy between statins and non-steroidal anti-inflammatory drugs in growth inhibition and apoptosis induction in cultured cancer cells. This study aimed at evaluating the combined anti-inflammatorty and apoptotic effects of atorvastatin and celecoxib in adjuvant-induced arthritis in rats. Adjuvant arthritis was induced in Sprague-Dawley rats by intradermal injection of 0.1 ml suspension of heat-killed Mycobacterium butyricum (12 mg/ml) in incomplete Freund's adjuvant. Rats were treated orally with atorvastatin (10 mg/kg/day), celecoxib (3 mg/kg/day) and their combination from day 12 to day 27 post-adjuvant injection. Arthritis progression was assessed by hind paw swelling and arthrogram scores. Serum levels of C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), interleukin-10 (IL-10) and vascular endothelial growth factor (VEGF) were measured. Caspase-3 activity and DNA fragmentation were determined in tibiotarsal joints tissue to evaluate apoptosis. Celecoxib proved to be more effective, than atorvastatin in suppressing clinical severity of arthritis, reducing serum levels of VEGF, CRP and TNF-α and increasing serum levels of IL-10. Caspase-3 activity and DNA fragmentation were more significantly enhanced by atorvastatin.	2013	

			Combining atorvastatin and celecoxib provided higher efficacy, in reducing inflammation and inducing apoptosis, than either agent alone.		
2	Astrocyte-Targeted Transporter-Utilizing Derivatives of Ferulic Acid Can Have Multifunctional Effects Ameliorating Inflammation and Oxidative Stress in the Brain. Oxidative medicine and cellular longevity. 2019. https://doi.org/10.1155/2019/3528148.	Drug targeting	Ferulic acid (FA) is a natural phenolic antioxidant, which can exert also several other beneficial effects to combat neuroinflammation and neurodegenerative diseases, such as Alzheimer's disease. One of these properties is the inhibition of several enzymes and factors, such as β-site amyloid precursor protein (APP) cleaving enzyme 1 (BACE1), cyclooxygenases (COXs), lipoxygenases (LOXs), mammalian (or mechanistic) target for rapamycin (mTOR), and transcription factor NF-κB. We have previously synthesized three L-type amino acid transporter 1- (LAT1-) utilizing FA-derivatives with the aim to develop brain-targeted prodrugs of FA. In the present study, the cellular uptake and bioavailability of these FA-derivatives were evaluated in mouse primary astrocytic cell cultures together with their inhibitory effects towards BACE1, COX/LOX, mTOR, NF-κB, acetylcholinesterase (AChE), and oxidative stress. According to the results, all three FA-derivatives were taken up 200–600 times more effectively at 10 μM concentration into the astrocytes than FA, with one derivative having a high intracellular bioavailability ($K_{p,uu}$), particularly at low concentrations. Moreover, all of the derivatives were able to inhibit BACE1, COX/LOX, AChE, and oxidative stress measured as decreased cellular lipid peroxidation. Furthermore, one of the derivatives modified the total mTOR amount. Therefore, these derivatives have the potential to act as multifunctional compounds preventing β-amyloid accumulation as well as combating inflammation and reducing oxidative stress in the brain. Thus, this	2019	https://onlinelibrary.wiley.com/doi/full/10.1155/2019/3528148

			study shows that converting a parent drug into a transporter-utilizing derivative not only may increase its brain and cellular uptake, and bioavailability but can also broaden the spectrum of pharmacological effects elicited by the derivative.		
3	Sitagliptin and tofacitinib ameliorate adjuvant induced arthritis via modulating the cross talk between JAK/STAT and TLR-4/NF-κB signaling pathways. Life Sciences. 2020. https://doi.org/10.1016/j.lfs.2020.118261.	Drug repurposing In Rheumatoid arthritis (autoimmune disorder)	**Aims** Rheumatoid arthritis is an autoimmune systemic disorder causing pain, swelling, stiffness, and disability in various joints. This work was designed to evaluate the effect of sitagliptin and tofacitinib on Janus kinase (JAK)/signaling transducer and activator of transcription (STAT) and toll like receptor (TLR-4)/nuclear factor kappa B (NF-κB) signaling pathways in adjuvant induced arthritis in rats. **Materials and methods** Severity of arthritis was evaluated and serum was analyzed for inflammatory mediators. The mRNA and protein expression level of the most important members of the two signaling pathways were determined. Lipid profile, transaminases and renal function parameters were assessed. **Key findings** Sitagliptin and tofacitinib significantly decreased the level of inflammatory parameters, the mRNA and protein expression level of the members of JAK/STAT and TLR-4/NF-κB pathways with more prominent effect of sitagliptin on TLR-4/NF-κB pathway and more expected obvious effect of tofacitinib on JAK/STAT pathway. The combination offered additional anti-inflammatory effect by inhibiting the cross talk between these pathways as inhibition of NF-κB activation decreased the serum	2020	https://www.sciencedirect.com/science/article/abs/pii/S0024320520310134

			level of IL-6 preventing the activation of STAT-3 in tibiotarsal tissues. **Significance** The combination of tofacitinib and sitagliptin normalized serum lipids and blood glucose level which could offer protection against cardiovascular diseases and caused partial reversal of serum transaminases and creatinine levels which can protect against tofacitinb's related hepato and nephrotoxicity. We could conclude that the combination of Sitagliptin with tofacitinib can offer synergistic anti-inflammatory effect and more protective action against side effects of tofacitinib.		
4	Metformin and omega-3 fish oil elicit anti-inflammatory effects via modulation of some dysregulated micro RNAs expression and signaling pathways in experimental induced arthritis. International Immunopharmacology.2021. https://doi.org/10.1016/j.intimp.2020.107362.	Drug repurposing in Rheumatoid arthritis (autoimmune disorder)	**Objective** Rheumatoid arthritis is a progressive inflammatory disease with multiple dysfunctional intracellular signaling pathways that necessitate new approaches for its management. Hence, the study aimed to inspect the ability of the combination therapy of metformin and omega-3 to modulate different signaling pathways and micro RNAs such as (miR-155, miR-146a and miR-34) as new targets in order to mitigate adjuvant-induced arthritis and compare their effect to that of methotrexate. **Methods** Fourteen days post adjuvant injection, Sprague-Dawley rats were treated orally with metformin (200 mg/kg/day) and/or omega-3 (300 mg/kg/day) or intraperitoneally with methotrexate (2 mg/kg/week) for 4 weeks. **Results and conclusion** All drug treatments amended the arthrogram score and hind paw swelling as well as decreased serum tumor necrosis factor (TNF)-α and interleukin (IL)-	2021	https://www.sciencedirect.com/science/article/abs/pii/S1567576920338303

			1β levels. On the molecular level, all therapies activated phospho-5′adenosine monophosphate-activated protein kinase (p-AMPK) and protein phosphatase 2A (PP2A), while they inhibited phospho-mammalian target of rapamycin (p-mTOR), phospho-signal transducers and activators of transcription (p-STAT3), nuclear factor (NF)-κB p65 subunit, phosho38 mitogen-activated protein kinase (p38 MAPK) and phospho- c-Jun N-terminal kinase (p-JNK). In addition, they decreased the elevated expression level of miRNA-155, 146a and increased the expression level of miRNA-34 and they decreased the expression level of retinoic acid receptor related orphan receptor γT (RORγT) and increased that of fork head box P3 (FOXP3), correcting Th17/Treg cells balance. On most of the aforementioned parameters, the effect of the combination therapy was comparable to that of methotrexate, emphasizing that this combination possesses better additive anti-inflammatory effect than either drug when used alone. In addition, the combination was capable of normalizing the serum transaminases levels as compared to untreated group offering hepatoprotective effect and suggesting the possibility of its use as a replacement therapeutic strategy for MTX in rheumatoid arthritis.		
5	Orchestrated modulation of rheumatoid arthritis via crosstalking intracellular signaling pathways. Inflammopharmacology.2021. https://doi.org/10.1007/s10787-021-00800-3	Molecular targeting in Rheumatoid arthritis (autoimmune disorder)	Cell signaling is considered a part of a network for communication that regulates basic cellular activities. The ability of cells to communicate correctly to the surrounding environment has an important role in development, tissue repair, and immunity as well as normal tissue homeostasis. Dysregulated activation and crosstalk between many intracellular signaling pathways are implicated in the pathogenesis of rheumatoid arthritis (RA), such as the Janus Kinase/signal transducers and activators of	2021	https://link.springer.com/article/10.1007/s10787-021-00800-3

			transcription (JAK/STAT), Toll-like receptor/nuclear factor kappa B (TLR/NF-κB), phosphatidylinositide-3Kinase/protein kinase B/mammalian target of rapamycin (PI-3K/AKT/mTOR), the stress activated protein kinase/mitogen-activated protein kinase (SAPK/MAPK), and spleen tyrosine kinase (SYK) pathways. Other interrelated pathways that can be targeted to halt the inflammatory status in the disease are purinergic 2X7 receptor (P2X7R)/nucleotide binding oligomerization domain-like receptor family pyrin domain containing 3 or inflammasome (NLRP-3)/NF-κB and Notch pathways. In this review, we will show the orchestrated modulation in the pathogenesis of RA via the crossregulation between dysregulated signaling pathways which can mediate a sustained loop of activation for these signaling pathways as well as aggrevate the inflammatory condition. Also, this review will highlight many targets that can be useful in the development of more effective therapeutic options.		
6	Micro RNAs 26b, 20a inversely correlate with GSK-3 β/NF-κB/NLRP-3 pathway to highlight the additive promising effects of atorvastatin and quercetin in experimental induced arthritis. International Immunopharmacology. 2021 https://doi.org/10.1016/j.intimp.2021.108042.	Drug repurposing in Rheumatoid arthritis (autoimmune disorder)	Rheumatoid arthritis (RA) is an inflammatory disease with challenging therapeutic potential due to the implication of cross-talking intracellular pathways in the pathogenesis of the disease. This study aimed to evaluate the effects of the combination therapy of atorvastatin and quercetin on glycogen synthase kinase-3 beta/ nuclear factor kappa-B/ nucleotide-binding oligomerization domain-like receptor family pyrin domain containing-3 or inflammasome (GSK-3β/NF-KB/NLRP-3) pathway as well as on microRNAs 26b and 20a (miR-26b, miR-20a) and to investigate the possible beneficial outcomes of the combination to offer a better treatment option than methotrexate (MTX) in adjuvant-induced arthritis (AIA).	2021	https://www.sciencedirect.com/science/article/abs/pii/S1567576921006780

			Assessment of arthritis progression, serum inflammatory, and oxidative parameters were done. The tibiotarsal tissue expression of the inflammatory parameters was evaluated. Western blot analysis was done to assess the expression level of the important members in the GSK-3β/NF-κB/NLRP-3 pathway. Furthermore, the expression level of both microRNAs and serum level of transaminases were determined. All treatments, especially the combination regimen, abated arthritis progression, the elevated serum level of inflammatory and oxidative stress parameters in arthritic rats. Moreover, They down-regulated the gene expression of the important members of the aforementioned signaling pathway, amended the tissue levels of inflammatory parameters and elevated the expression level of miR-26b and miR-20a. Finally, we concluded that the combination therapy modulated miR-26b and miR-20a as well as GSK-3β/NF-κB/NLRP-3 pathway, provided additive anti-inflammatory and anti-oxidant effects and offered an additional hepatoprotective effect as compared to untreated arthritic rats and MTX-treated groups, suggesting its promising role to be used as replacement therapy to MTX in RA.		
7	Anti-neoplastic action of Cimetidine/Vitamin C on histamine and the PI3K/AKT/mTOR pathway in Ehrlich breast cancer. Scientific reports. 2022. https://doi.org/10.1038/s41598-022-15551-6.	Drug repurposing in Breast cancer	The main focus of our study is to assess the anti-cancer activity of cimetidine and vitamin C via combating the tumor supportive role of mast cell mediators (histamine, VEGF, and TNF-α) within the tumor microenvironment and their effect on the protein kinase A(PKA)/insulin receptor substrate-1(IRS-1)/phosphatidylinositol-3-kinase (PI3K)/serine/threonine kinase-1 (AKT)/mammalian target of rapamycin (mTOR) cue in Ehrlich induced breast cancer in mice. In vitro study was carried out to evaluate the anti-	2022	https://www.nature.com/articles/s41598-022-15551-6

			proliferative activity and combination index (CI) of the combined drugs. Moreover, the Ehrlich model was induced in mice via subcutaneous injection of Ehrlich ascites carcinoma cells (EAC) in the mammary fat pad, and then they were left for 9 days to develop obvious solid breast tumor. The combination therapy possessed the best anti-proliferative effect, and a CI < 1 in the MCF7 cell line indicates a synergistic type of drug interaction. Regarding the in vivo study, the combination abated the elevation in the tumor volume, and serum tumor marker carcinoembryonic antigen (CEA) level. The serum vascular endothelial growth factor (VEGF) level and immunohistochemical staining for CD34 as markers of angiogenesis were mitigated. Additionally, it reverted the state of oxidative stress and inflammation. Meanwhile, it caused an increment in apoptosis, which prevents tumor survival. Furthermore, it tackled the elevated histamine and cyclic adenosine monophosphate (cAMP) levels, preventing the activation of the (PKA/IRS-1/PI3K/AKT/mTOR) cue. Finally, we concluded that the synergistic combination provided a promising anti-neoplastic effect via reducing the angiogenesis, oxidative stress, increasing apoptosis,as well as inhibiting the activation of PI3K/AKT/mTOR cue, and suggesting its use as a treatment option for breast cancer.		
8	Galangin Mitigates DOX-induced Cognitive Impairment in Rats: Implication of NOX-1/Nrf-2/HMGB1/TLR4 and TNF-α/MAPKs/RIPK/MLKL/BDNF. Neurotoxicology.2022. https://doi.org/10.1016/j.neuro.2022.07.005.	Drug repurposing in treatment of Neurotoxicity	The cognitive and behavioral decline observed in cancer survivors who underwent doxorubicin (DOX)-based treatment raises the need for therapeutic interventions to counteract these complications. Galangin (GAL) is a flavonoid-based phytochemical with pronounced protective effects in various neurological disorders. However, its impact on DOX-provoked neurotoxicity has not been	2022	https://www.sciencedirect.com/science/article/abs/pii/S0161813X22001206

			clarified. Hence, the current investigation aimed to explore the ability of GAL to ameliorate DOX-provoked chemo-brain in rats. DOX (2 mg/kg, once/week, i.p.) and GAL (50 mg/kg, 5 times/week., via gavage) were administered for four successive weeks. The MWM and EPM tests were used to evaluate memory disruption and anxiety-like behavior, respectively. Meanwhile, targeted biochemical markers and molecular signals were examined by the aid of ELISA, Western blotting, and immune-histochemistry. In contrast to DOX-impaired rats, GAL effectively preserved hippocampal neurons, improved cognitive/behavioral functions, and enhanced the expression of the cell repair/growth index, BDNF. The antioxidant feature of GAL was confirmed by the amelioration of MDA, NO and NOX-1, along with restoring the Nrf-2/HO-1/GSH cue. In addition, GAL displayed marked anti-inflammatory properties as verified by the suppression of the HMGB1/TLR4 nexus and p-NF-κB p65 to inhibit TNF-α, IL-6, IL-1β, and iNOS. This inhibitory impact extended to entail astrocyte activation, as evidenced by the diminution of GFAP. These beneficial effects were associated with a notable reduction in p-p38MAPK, p-JNK1/2, and p-ERK1/2, as well as the necroptosis cascade p-RIPK1/p-RIPK3/p-MLKL. Together, these pleiotropic protective impacts advocate the concurrent use of GAL as an adjuvant agent for managing DOX-driven neurodegeneration and cognitive/behavioral deficits.		
9	Possible Implication of Nrf2, PPAR-γ and MAPKs Signaling in the Protective Role of Mangiferin against Renal Ischemia/Reperfusion in Rats".	Natural agents repurposing in Ischemia/Reperfusion in Rats	Mangiferin (Mang) is a known glucosylxanthone that has proven its shielding effect against ischemia/reperfusion (Is/R). However, its full underlying mechanistic perspective against renal Is/R induced lesions is not fully revealed.	2022	https://www.mdpi.com/1424-8247/16/1/6

	Pharmaceuticals. 2022. https://doi.org/10.3390/ph16010006		Consequently, the purpose of this study is to track further non-investigated modulatory signals of Mang against the renal Is/R model involving nuclear factor erythroid 2-related factor (Nrf)2/heme oxygenase (HO)-1, peroxisome proliferator-activated receptor (PPAR)-γ/nuclear factor (NF)-κB, p38 mitogen-activated protein kinase (MAPK), and c-Jun N-terminal kinase (JNK) signaling. To ratify our aim, Mang was administrated (20 mg/kg, i.p for seven days) before the induction of bilateral Is/R. Mechanistic maneuver revealed that Mang balanced oxidative state via increasing the expression of the antioxidant Nrf2/HO-1 cue with subsequent enhancement of GSH besides MDA lessening. Additionally, Mang enhanced PPAR-γ mRNA expression and declined *p*-p38 MAPK and *p*-JNK expression with concomitant NF-κB downsizing leading to iNOS/NOx and TNF-α rebating. Furthermore, the Mang anti-apoptotic trait was affirmed by enriching Bcl-2 expression as well as decreasing Bax and caspase-3 expression. All these potentials were in the line with the molecular docking results and the improved histopathological findings and renal function biomarkers. Consequently, Mang provided plausible protective mechanisms against renal Is/R-related events, possibly by amending oxidative status, inflammatory mediators, and apoptotic cell death through the involvement of Nrf2, PPAR-γ, MAPK, JNK, and NF-κB signaling.		
10	Gastroprotective and anti-Helicobacter pylori potentials of essential oils from the oleoresins of Araucaria bidwillii and Araucaria heterophylla. Inflammopharmacology. 2022. https://doi.org/10.1007/s10787-022-01112-w.	Natural agents repurposing in Gastric injury	Plant resins or oleoresins comprise a chemically complex mixture of different classes of compounds. Oleoresin of the genus Araucaria combines essential oil (EO) and resin. It possesses gastroprotective, cytotoxic, and timicrobial, antipyretic, and anti-inflammatory activities. The study aimed to	2022	https://link.springer.com/article/10.1007/s10787-022-01112-w

			investigate the EOs from the oleoresins of two Araucaria species, A. bidwillii and A. heterophylla, chemically and biologically for their gastroprotective, anti-inflammatory, antioxidant, and anti-Helicobacter pylori potentials. The chemical composition of both species cultivated in Egypt was analyzed with GC-MS and compared with those cultivated abroad using principal component analysis (PCA). There were 37 and 17 secondary metabolites identified in A. heterophylla and A. bidwillii, respectively. The EOs of both species showed a pronounced inhibitory effect on Helicobacter pylori activity in vitro. The gastroprotective effect was assessed in vivo using ethanol-induced gastric ulcer model in rats. Inflammatory cytokines, oxidative stress, and the nuclear factor-kappa B (NF-κB) biomarkers were assessed in the stomach tissues. The ulcer index and percentage of ulcer protection were determined. Stomach sections were examined histopathologically by staining with (H/E) and periodic acid Schiff (PAS). Moreover, the proliferative index was determined using the Ki-67 immunostaining. The treatment of rats with EOs (50, 100, and 200 mg/kg, orally) 1 hour prior to ethanol administration showed promising gastroprotective, anti-inflammatory, and antioxidant potentials. These findings declared the gastroprotective role played by both EOs with the superiority of A. bidwillii over A. heterophylla via modulation of oxidative stress/NF-κB/inflammatory cytokines. Their use can be recommended to protect against the recurrence of peptic ulcers.		
11	Diosmin nanocrystals alleviate Imiquimod induced psoriasis in rats via modulating TLR7, 8/NF-κB/micro RNA-31, AKT/mTOR/P70S6K	Drug nano-formulation in psoriasis	Diosmin is a flavonoid with promising anti-inflammatory and antioxidant properties. However, it has difficult physicochemical characteristics since its solubility demands a pH level of 12, which has an	2022	https://link.springer.com/article/10.1007/s10787-023-01198-w

	milieu and Tregs/Th17 balance. Inflammopharmacology.2022.		impact on the drug's bioavailability. The aim of this work is the development and characterization of diosmin nanocrystals using anti-solvent precipitation technique to be used for topical treatment of psoriasis. Results revealed that diosmin nanocrystals stabilized with hydroxypropyl methylcellulose (HPMC E15) in ratio (diosmin:polymer; 1:1) reached the desired particle size (276.9 ± 16.49 nm); provided promising colloidal properties and possessed high drug release profile. Additionally, in-vivo assessment was carried out to evaluate and compare the activities of diosmin nanocrystal gel using three different doses and diosmin powder gel in alleviating imiquimod-induced psoriasis in rats and investigating their possible anti-inflammatory mechanisms. Herein, 125 mg of 5% imiquimod cream (IMQ) was applied topically for 5 consecutive days on the shaved backs of rats to induce psoriasis. Diosmin nanocrystal gel especially in the highest dose used offered the best anti-inflammatory effect. This was confirmed by causing the most statistically significant reduction in the psoriasis area severity index (PASI) score and the serum inflammatory cytokines levels. Furthermore, it was capable of maintaining the balance between T helper (Th17) and T regulatory (Treg) cells. Moreover, it tackled TLR7/8/NF-κB, miRNA-31, AKT/mTOR/P70S6K and elevated the TNFAIP3/A20 (a negative regulator of NF-κB) expression in psoriatic skin tissues. This highlights the role of diosmin nanocrystal gel in tackling imiquimod-induced psoriasis in rats, and thus it could be a novel promising therapy for psoriasis.		

12	Gastroprotective potential of red onion (Allium cepa L.) peel in ethanol-induced gastric injury in rats: Involvement of Nrf2/HO-1 and HMGB-1/NF-κB trajectories. J Ethnopharmacol. 2023 Aug 31:117115. doi: 10.1016/j.jep.2023.117115.	Natural agents repurposing in gastric injury	**Ethnopharmacological relevance** The utilization of plants with therapeutic properties in traditional medicine has a longstanding practice. Among them, the well-known *Allium cepa* L. commonly known as onion has been valued for its anti-inflammatory and antioxidant potential in the treatment of various ailments, including gastric ulcers. **Aim of the study** This study investigated the gastroprotective potential of red onion peel extract and its fractions in a rat model of ethanol-induced gastric ulcer. Moreover, their phytochemical profiles were compared to identify the active metabolites. **Materials and methods** Mass spectrometry-based metabolomics and chemometrics were performed for phytochemical analysis. Ethanol-induced gastric ulcer model was used to assess the gastroprotective activity. Nine groups of rats were allocated as follows: Group 1 was the normal control; Group 2 rats were used as a positive control/model and received 1 mL of absolute ethanol; and Group 3 rats were treated with famotidine at a dose of 20 mg/kg orally. Group 4 and 5 rats were treated with total acidified ethanolic extract (T1, T2). Group 6 and 7 rats were treated with anthocyanins-rich fractions (P1, P2). Groups 8 and 9 were the flavonoids-rich fraction (S1, S2) treatment. Prior to scarification, the ulcer index in mm was obtained from gastric tissues photographed beside a ruler with further analysis using ImageJ software. **Results** Seventy key major and discriminatory metabolites were identified including flavonoids, anthocyanins, phenolic acids, and miscellaneous compounds. The	2023	https://www.sciencedirect.com/science/article/abs/pii/S0378874123009832

			examined extract and its fractions significantly reduced the ulcer index and inflammatory cytokines *via* downregulating HMGB-1/NF-κB. Also, they augmented the expression of Nrf2/HO-1 and reduced NOX1/4 mRNA expression. Moreover, there was a significant reduction in the oxidative stress and apoptotic biomarkers as well as a noticeable enhancement in histopathological changes of the stomach tissues. **Conclusion** Red onion peels have a promising dose dependent gastroprotective potential in alcohol-induced ulcers *via* modulating Nrf2/HO-1 and HMGB-1/NF-κB trajectories. This highlights the potential of red onion peels in treating gastric ulcers.		
13	L-Carnitine augments probenecid anti-inflammatory effect in monoiodoacetate-induced knee osteoarthritis in rats: involvement of miRNA-373/P2X7/NLRP3/NF-κB milieu. Inflammopharmacology. 2023. https://doi.org/10.1007/s10787-023-01376-w.	Drug repurposing in osteoarthritis	Osteoarthritis (OA) is a degenerative joint disease, whereas the underlying molecular trails involved in its pathogenesis are not fully elucidated. Hence, the current study aimed to investigate the role of miRNA-373/P2X7/NLRP3/NF-κB trajectory in its pathogenesis as well as the possible anti-inflammatory effects of probenecid and l-carnitine in ameliorating osteoarthritis via modulating this pathway. In the current study, male Sprague Dawley rats were used and monoiodoacetate (MIA)-induced knee osteoarthritis model was adopted. Probenecid and/or L-carnitine treatments for 14 days succeeded in reducing OA knee size and reestablishing motor coordination and joint mobility assessed by rotarod testing. Moreover, different treatments suppressed the elevated serum levels of IL-1β, IL-18, IL-6, and TNF-α via tackling the miRNA-373/P2X7/NLRP3/NF-κB, witnessed as reductions in protein expressions of P2X7, NLRP3, cleaved caspase-1 and NF-κB. These were accompanied by	2023	https://link.springer.com/article/10.1007/s10787-023-01376-w

			increases in procaspase-1 and IκB protein expression and in miRNA-373 gene expression OA knee to various extents. In addition, different regimens reversed the abnormalities observed in the H and E as well as Safranin O-Fast green OA knees stained sections. Probenecid or l-carnitine solely showed comparable results on the aforementioned parameters, whereas the combination therapy had the most prominent effect on ameliorating the aforementioned parameters. In conclusion, l-carnitine augmented the probenecid's anti-inflammatory effect to attenuate MIA-induced osteoarthritis in rats by provoking the miRNA-373 level and inhibiting the P2X7/NLRP3/NF-κB milieu, leading to the suppression of serum inflammatory cytokines: IL-1β, IL-18, IL-6, and TNF-α. These findings suggest the possibility of using probenecid and l-carnitine as a useful therapeutic option for treatment of osteoarthritis.		
14	Antioxidant and anti-Alzheimer activities of Clivia miniata (Lindl) roots, bulbs, and aerial parts: In-vitro and in-silico studies. Biomedicine & Pharmacotherapy 2023. doi.org/10.1016/j.biopha.2023.115382.	Natural agents repurposing in neuroscience	*Clivia miniata* (Lindl) is a member of the family Amaryllidaceae known for its chemically diverse alkaloids with a wide range of biological activities. Many reports revealed a direct role of oxidative stress in the early stage of Alzheimer's disease (AD). Meanwhile, β-site amyloid precursor protein cleavage enzyme 1 (BACE-1) is a molecular target for the treatment of AD. We aimed to investigate *C. miniata* root, bulb, and aerial part chemical profiling, antioxidant, BACE-1, and AChE enzyme inhibitory activities. Results showed that the total root had the most potent radical scavenging activity as compared to the total bulb and aerial part, respectively. Ethanol root extract had the most potent BACE-1 inhibitory activity (IC_{50} = 0.02 ± 0.001 µg/mL) as compared to the bulb and aerial part (IC_{50} = 0.93 ± 0.13, 1.80 ± 0.24 µg/mL),	2023	https://www.sciencedirect.com/science/article/pii/S0753332223011794

			respectively. Moreover, the total root extract mitigated AChE enzyme activity more than total bulb and aerial fractions with IC_{50} values of (0.06 ± 0.02, 0.58 ± 0.3, and 1.89 ± 0.42 µg/mL, respectively. Bioassay-guided acid-base fractionation confirmed superior BACE-1 inhibitory activity of the root fractions particularly, methylene chloride and ethyl acetate fractions with (IC_{50} values of 0.21 ± 0.60 and 0.01 ± 0.001 µg/mL), respectively. UPLC-MS analysis of ethyl acetate and methylene chloride fractions of *C. miniata* root led to the identification of eight phenolics and thirteen alkaloids, respectively. Molecular docking studies against BACE-1 protein revealed that lycorine di-hexoside, miniatine, and cliviaaline were the most promising hits. Further investigation of anti-AD potential of the aforementioned small molecules is required.		
15	Enhancing collagen based nanoemulgel for effective topical delivery of Aceclofenac and Citronellol oil: Formulation, optimization, in-vitro evaluation, and in-vivo osteoarthritis study with a focus on HMGB-1/RAGE/NF-κB pathway, Klotho, and miR-499a. Drug Delivery and Translational Research 2024. doi.org/10.1007/s13346-024-01548-3	Drug nano-formulation in osteoarthritis	The majority of conventional osteoarthritis (OA) treatments are based on molecular adjustment of certain signaling pathways associated with osteoarthritis (OA) pathogenesis, however there is a significant need to search for more effective and safe treatments. This study centers around formulating Aceclofenac (ACF) with high bioavailability in combination with Citronellol oil and collagen. The optimal concentrations of Citronellol oil/D-Limonene oil, Tween 80, and Transcutol HP were determined using a pseudoternary phase diagram. The formulated nanoemulsions were studied for thermophysical stability. Thermodynamically stable formula were analyzed for droplet size, zeta potential, and in-vitro permeation. Then, collagen based nanoemulsion were prepared to capitalize on its efficacy in reducing osteoarthritis side effects and characterized for nano size properties. Formulae F10	2024	https://link.springer.com/article/10.1007/s13346-024-01548-3

			and F10C were chosen as optimum nanosize formula. Hense, they were prepared and characterized as nanoemulgel dosage form. The nanoemulgel formulae F10NEG1 and F10CNEG1 showed reasonable viscosity and spreadability, with complete drug release after 4 h. These formulae were chosen for further In vivo anti-OA study. Collagen based ACF/citronellol emugel were able to modulate HMGB-1/RAGE/NF-κB pathway, mitigating the production of inflammatory cytokine TNF-α. They were also able to modulate Klotho and miR-499, reducing serum CTXII and COMP, by reducing the cartilage destruction. Histological investigations validated the efficacy, safety, and superiority of Aceclofenac in combination with Citronellol oil and collagen (F10CNEG1) over solo the treated group (F10NEG1 and blank). Hence, the findings of the current work encourage the use of this promising combined formula in treatment of OA patients.		
16	A drug repurposing approach of Atorvastatin calcium for its antiproliferative activity for effective treatment of breast cancer: In vitro and in vivo assessment. International Journal of Pharmaceutics: X 2024. doi.org/10.1016/j.ijpx.2024.100249.	drug repurposing in breast cancer	Breast cancer, the most common cancer among women, caused over 500,000 deaths in 2020. Conventional treatments are expensive and have severe side effects. Drug repurposing is a novel approach aiming to reposition clinically approved non-cancer drugs into newer cancer treatments. Atorvastatin calcium (ATR Ca) which is used for the treatment of hypercholesterolemia has potential to modulate cell growth and apoptosis. The study aimed at utilizing gelucire-based solid lipid nanoparticles (SLNs) and lactoferrin (Lf) as targeting ligand to enhance tumor targeting of atorvastatin calcium for effective management of breast cancer. Lf-decorated-ATR Ca-SLNs showed acceptable particle size and PDI values <200 nm and 0.35 respectively, entrapment efficiency >90% and sustained drug release profile with 78.97 ± 12.3% released after 24	2024	https://www.sciencedirect.com/science/article/pii/S2590156724000215

			h. In vitro cytotoxicity study on breast cancer cell lines (MCF-7) showed that Lf-decorated-ATR Ca-SLNs obviously improved anti-tumor activity by 2 to 2.5 folds compared to undecorated ATR Ca-SLNs and free drug. Further, In vivo study was also carried out using Ehrlich breast cancer model in mice. Caspase-3 apoptotic marker revealed superior antineoplastic and apoptosis-inducing activity in the groups treated with ATR Ca-SLNs either decorated/ undecorated with Lf in dosage 10 mg/kg/day $p < 0.001$ with superior activity for lactoferrin-decorated formulation.		
17	Boswellic acid and apigenin alleviate methotrexate-provoked renal and hippocampal alterations in rats: Targeting autophagy, NOD-2/NF-κB/NLRP3, and connexin-43. International Immunopharmacology 2024. doi.org/10.1016/j.intimp.2024.112147.	Drug repurposing to alleviate MTX induced renal and hippocampal side effects	The neuronal and renal deteriorations observed in patients exposed to methotrexate (MTX) therapy highlight the need for medical interventions to counteract these complications. Boswellic acid (BA) and apigenin (APG) are natural phytochemicals with prominent neuronal and renal protective impacts in various ailments. However, their impacts on MTX-provoked renal and hippocampal toxicity have not been reported. Thus, the present work is tailored to clarify the ability of BA and APG to counteract MTX-provoked hippocampal and renal toxicity. BA (250 mg/kg) or APG (20 mg/kg) were administered orally in rats once a day for 10 days, while MTX (20 mg/kg, i.p.) was administered once on the sixth day of the study. At the histopathological level, BA and APG attenuated MTX-provoked renal and hippocampal aberrations. They also inhibited astrocyte activation, as proven by the inhibition of glial fibrillary acidic protein (GFAP). These impacts were partially mediated *via* the activation of autophagy flux, as proven by the increased expression of beclin1, LC3-II, and the curbing of p62 protein, alongside the regulation of the *p*-AMPK/mTOR nexus. In addition, BA and APG	2024	https://www.sciencedirect.com/science/article/abs/pii/S1567576924006659

			displayed anti-inflammatory features as verified by the damping of NOD-2 and *p*-NF-κB p65 to reduce TNF-α, IL-6, and NLRP3/IL-1β cue. These promising effects were accompanied with a notable reduction in one of the gap junction proteins, connexin-43 (Conx-43). These positive impacts endorse BA and APG as adjuvant modulators to control MTX-driven hippocampal and nephrotoxicity.		
18	The gastroprotective effect of Yucca filamentosa standardized crude leaves extract versus its nano - cubosomal formulation in ethanol-induced gastric injury. International Immunopharmacology 2024.	Natural agent repurposing in gastric injury	Yucca filamentosa (YF) is widely used in folk medicine for its anti-inflammatory effects. Our study aimed to evaluate the chemical profile of YF extracts. Additionally, the gastroprotective efficacy of its crude leaf extract and nano-cubosomal formulation was assessed in a rat model of ethanol-induced gastric injury by altering the HMGB-1/RAGE/TLR4/NF-κB pathway. The phytochemical composition of YF was investigated using FTIR spectroscopy and LC-MS/MS techniques. Standardization was further accomplished using HPLC. Rats were treated orally with yucca crude extract or its nano-cubosomal formulation at doses of 25, 50, and 100 mg/kg. Famotidine (50 mg/kg, IP) was used as a reference drug. After 1 h, rats were administered ethanol (1 ml, 95 %, orally). One hour later, the rats were sacrificed, and the serum was separated to determine TNF-α and IL-6 levels. Stomachs were excised for the calculation of the ulcer index and histopathological examinations. Stomach tissue homogenate was used to determine MDA and catalase levels. Additionally, the expression levels of HMGB-1/RAGE/TLR4/NF-κB were assessed.	2024	https://www.sciencedirect.com/science/article/abs/pii/S1567576924009615

			Phytochemical analysis confirmed the predominance of steroidal saponins, sucrose, organic and phenolic acids, and kaempferol. The nano-cubosomal formulation demonstrated enhanced gastroprotective, anti-oxidant, and anti-inflammatory efficacy compared to the crude extract at all tested doses. The most prominent effect was observed in rats pretreated with the YF nano-cubosomal formulation at a dose of 100 mg/kg, which was similar to normal control and famotidine-treated rats. Our results highlighted the enhanced gastroprotective impact of the yucca nano-cubosomal formulation in a dose-dependent manner. This suggests its potential use in preventing peptic ulcer recurrence.		
19	Tetrandrine ameliorated atherosclerosis in vitamin D3/high cholesterol diet-challenged rats via modulation of miR-34a and Wnt5a/Ror2/ABCA1/NF-kB trajectory Scientific reports	Natural agent repurposing in atherosclerosis treatment	Atherosclerosis (AS) is a major cause of cardiovascular diseases that may lead to mortality. This study aimed to evaluate the therapeutic potential of tetrandrine in high cholesterol diet (HCD)-induced atherosclerosis, in rats, via modulation of miR-34a, as well as, Wnt5a/Ror2/ABCA1/NF-κB pathway and to compare its efficacy with atorvastatin. Induction of AS, in male rats, was done via IP administration of vitamin D3 (70 U/Kg for 3 days) together with HCD. At the end of the 9th week, rats were treated with atorvastatin at a dose of 20 mg/kg, and tetrandrine at different doses of (18.75, and 31.25 mg/kg) for 22 days. Serum inflammatory cytokines and lipid profile, liver oxidative stress parameters, and aortic tissue Wnt5a, Ror2, ABCA1, NF-κB, miR-34a levels were assessed in all experimental groups. Histopathological and Immunohistochemical assessments of aortic tissue sections were done.	2024	In press

			Results showed that tetrandrine treatment reverted the inflammatory and oxidative stress state together with reducing the serum lipids via modulating miR-34a, and Wnt5a/Ror2/ABCA1/NF-κB pathway. Moreover, it reverted the histopathological abnormalities observed in AS rats. Tetrandrine beneficial effects, in both doses, were comparable to that of atorvastatin, in most of the discussed parameters. These findings praise tetrandrine as a promising agent for management of atherosclerosis.		