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MINIREVIEWS

Glucagon-like peptide and its receptor agonists for the treatment of rheumatic diseases

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Abstract

Glucagon-like peptide-1 (GLP-1) and its receptor agonists (GLP-1RAs) are well-established therapies for metabolic conditions such as type 2 diabetes and obesity due to their ability to enhance insulin secretion, promote weight loss, and regulate blood glucose levels. Emerging evidence, however, indicates that GLP-1RAs may also have therapeutic potential in inflammatory and autoimmune conditions. This review explores the evolving role of GLP-1RAs in managing rheumatic diseases, including osteoarthritis, rheumatoid arthritis, psoriatic arthritis, and systemic lupus erythematosus. Studies suggest that GLP-1RAs reduce inflammation by modulating immune cell activity, increasing anti-inflammatory cytokine production, shifting macrophage polarization toward an anti-inflammatory phenotype, and enhancing regulatory T-cell function to maintain immune homeostasis. These immunomodulatory effects point toward a promising adjunctive strategy in current clinical practice for patients with rheumatic diseases, particularly those with metabolic comorbidities. Further clinical trials are warranted to validate these findings, clarify underlying mechanisms, and assess long-term safety, ultimately paving the way for novel treatment approaches in rheumatology.

Key Words: Glucagon-like peptide-1 agonists; Osteoarthritis; Rheumatoid arthritis; Psoriatic arthritis; System lupus erythematosus; Inflammation

Core Tip: Growing evidence suggests that glucagon-like peptide-1 and its receptor agonists could be an effective treatment option not only for metabolic disorders but also for a range of autoimmune and inflammatory diseases. They may protect cartilage and reduce joint inflammation, lower the levels of inflammatory cytokines, and help prevent further joint damage and address both the metabolic and inflammatory aspects, reducing cytokine levels and potentially improving disease outcomes.

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INTRODUCTION

Glucagon-like peptide-1 (GLP-1) is a peptide that is primarily produced by the endocrine cells in the gut in response to nutrient intake[1]. Its primary role tends to involve the regulation of metabolism by increasing the secretion of insulin while suppressing the release of glucagon to maintain physiological blood glucose levels[1]. On another note, this peptide regulates the motility of the enteric system while supporting weight loss[2]. Once it reaches the bloodstream, it is directly inactivated within seconds by the enzyme dipeptidyl peptidase-4 (DPP-4), which cleaves the peptide between positions 8 and 9, converting it into the truncated form GLP-1(9–36) amide. To counteract this physiological mechanism, new forms of GLP-1 receptor agonists (GLP-1RAs) have been designed to oppose the breakdown by DPP-4[3].

On a biocellular level, these molecules tend to bind to their receptors, which are G-protein coupled receptors; the latter will lead to an intracellular increase of cyclic adenosine monophosphate, thus activating the various cellular cascades[4]. The role of this molecule is established by its abundance in a wide range of tissues beyond the pancreas, including the lungs, stomach, intestines, heart, blood vessels, kidneys, both the central and peripheral nervous systems, ovaries, skin, and various immune cells[5].

In the past decade, new evidence suggests that this molecule tends to have anti-inflammatory properties, which was demonstrated by the reduction in inflammatory markers in the plasma[6]. Regulatory T cells and others have been found to express on their surfaces GLP-1Rs, which are the main cells responsible for downregulating an overdrive in the immune system and preserving immune tolerance[6]. They suppressed autoimmune reactions by inhibiting the activation of self-reactive T cells that could harm the body's tissues. Additionally, they increased the response and functionality of regulatory T cells, due to their direct role in stimulating the synthesis of anti-inflammatory cytokines such as interleukin 10 (IL-10) and transforming growth factor beta (TGF-β)[6]. On a cellular level, the polarization of macrophages has been stimulated by this molecule, shifting them from the inflammatory M1 phenotype to the anti-inflammatory M2 phenotype, which plays a vital role in tissue regeneration as well in reducing inflammation, as they produce cytokines like IL-10 and TGF-β[5]. These properties may offer therapeutic benefits for certain autoimmune disorders, independent of their effects on glucose regulation and weight management (Figure 1).

GLP-1RAS IN OSTEOARTHRITIS

Osteoarthritis (OA) is a degenerative joint disease characterized by progressive degradation of the cartilage cushioning the ends of bones, subchondral bone remodeling, and synovial inflammation, leading to joint stiffening and decreased motility[7].

Several factors contribute to the pathogenesis of OA, with obesity being the leading cause, alongside aging, mechanical stress, and genetic predisposition[7]. Since obesity is a major risk factor for both OA and diabetes, this has led to the exploration of GLP-1RA as a potential treatment for OA due to its weight loss and anti-inflammatory properties. GLP-1RA can improve OA outcomes by promoting weight loss, which reduces mechanical stress on the joints; however, its benefits extend beyond obesity management[8,9].

Studies on rat knee sections showed GLP-1RA in the articular chondrocytes. Stimulating these receptors reduces inflammation at the joint level and promotes matrix protection while preventing apoptosis of the chondrocytes[10,11]. For instance, liraglutide exhibits anti-apoptotic effects by activating the phosphoinositide 3-kinase/Akt pathway, which protects chondrocytes from endoplasmic reticulum stress-induced apoptosis[10]. Moreover, GLP-1RA limits the inflammation induced by nuclear factor kappa, thereby reducing the expression of proinflammatory mediators like tumor necrosis factor (TNF), C-C motif ligand 2, and IL-6[12]. Experiments on mouse chondrocytes also revealed the added role of liraglutide in reducing inflammation by decreasing mRNA expression of inducible nitric oxide synthase, matrix metallopeptidase 13, and ADAM metallopeptidase with thrombospondin type 1 motif 5, culminating in a reduction of IL-6, prostaglandin E2, and nitric oxide[13]. Another study on rats with OA showed that GLP-1R activation can reduce cartilage inflammation through the protein kinase A/cAMP response element-binding protein pathway[14].

Moreover, GLP-1RA anti-catabolic effects can reduce cartilage degradation through the downregulation of TNF-mediated expression of catabolic enzymes, hence preserving essential components of the extracellular matrix such as type II collagen and aggrecan[15].

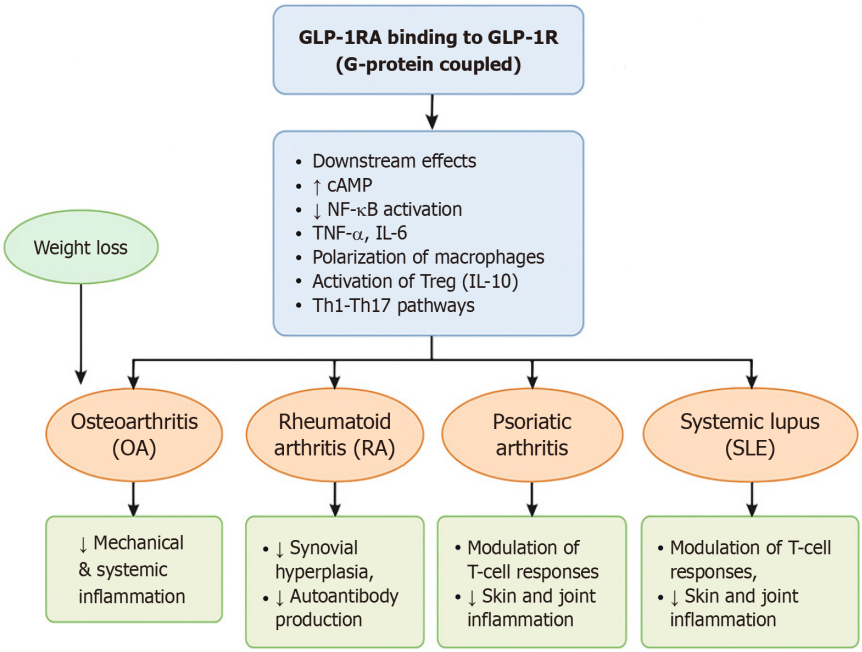

Figure 1 Mechanistic pathways of glucagon-like peptide-1 and its receptor agonists in rheumatic disease modulation. cAMP: Cyclic adenosine monophosphate; GLP-1RA: Glucagon-like peptide-1 and its receptor agonist(s); IL: Interleukin; NF-κB: Nuclear factor kappa B; Th: T helper type; TNF-α: Tumor necrosis factor-alpha.

RHEUMATOID ARTHRITIS AND GLP-1RAS

Rheumatoid arthritis (RA) is an autoimmune disorder characterized by chronic inflammation of the synovium, ultimately destroying bone and joint tissues, resulting in joint pain, swelling, and deformity[16]. Its pathogenesis involves a dysfunctional immune response whereby the immune system erroneously attacks synovial tissue[17]. Various inflammatory pathways are subsequently activated, leading to the release of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, which contribute to the ongoing joint damage through the perpetuation of chronic synovial inflammation[18].

Emerging evidence suggests that GLP-1RAs may be beneficial in the management of RA due to their anti-inflammatory and immunomodulatory properties[19]. *In vitro* studies have demonstrated the immunomodulatory activity of GLP-1RAs. Lixisenatide, for instance, has been shown to decrease pro-inflammatory cytokine production in human RA fibroblast-like synoviocytes (FLS)[19]. Following treatment initiation, a downregulation in TNF-α, IL-6, and IL-8 was noted, along with reduced tissue-degrading enzyme expression[20]. These anti-inflammatory effects were primarily linked to the suppression of key signaling pathways, such as c-Jun N-terminal kinase and activator protein 1.

GLP-1R activation has also been shown to suppress FLS proliferation and inhibit the p38 mitogen-activated protein kinase/nuclear factor kappa B (NF-κB) signaling pathway, leading to reduced inflammatory cytokine production and subsequent slowed tissue degradation[21].

Beyond their joint-specific effects, GLP-1RAs have demonstrated systemic anti-inflammatory properties by decreasing levels of C-reactive protein, IL-6, IL-1β, and TNF-α, and reducing macrophage infiltration into vascular tissues[22].

From a mechanistic perspective, GLP-1 appears to facilitate the differentiation of regulatory T cells (Tregs) while simultaneously inhibiting the responses of T helper 1 (Th1) cells and Th17 cells, both of which play a significant role in the pathogenesis of RA. Activation of the GLP-1R has been demonstrated to upregulate the expression of forkhead box p3 protein, a transcription factor crucial for Treg function, thus fostering immune tolerance and mitigating autoreactive inflammation[22,23]. Furthermore, treatment with GLP-1RAs resulted in decreased expression of T-box transcription factor TBX21 and retinoic acid-related orphan receptor gamma t, which are the principal transcription factors governing Th1 and Th17 differentiation, respectively[24]. These mechanisms lead to a diminished release of interferon gamma (IFN-) and IL-17—cytokines that are known to contribute to synovial inflammation and joint damage in RA[25,26]. This complex immunoregulatory action highlights the promise of GLP-1RAs as a potential disease-modifying therapy in the context of RA.

However, it is important to note that the precise molecular pathways through which GLP-1 modulates immune function in RA are not completely understood, as clinical trials addressing it are lacking. Future research should aim to address the therapeutic efficacy of GLP-1RAs in human trials and elucidate the mechanisms behind it.

SYSTEMIC LUPUS ERYTHEMATOSUS AND GLP-1RAS

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by systemic inflammation and multi-organ involvement. The pathogenesis of this disorder tends to be multifactorial, ranging from epigenetics to hormonal

imbalances and dysregulations[27]. The auto-activation of B cells in the body is responsible for the initiation of the disease, along with an imbalance between pro-inflammatory and anti-inflammatory immune responses[28]. The pathophysiological processes of SLE tend to be stimulated by a dysfunction in the immune system, both the innate and adaptive, leading to various tissue injuries through cytokine release and the deposition of immune complexes[29].

On a cellular level, this molecule counteracts the phosphorylation and the inactivation of inhibitor of kappa B alpha (IκBα), which is responsible for the sequestration of NF-κB in the cytoplasm, thus reducing the concentration of the pro-inflammatory cytokines that are primarily involved in the pathogenesis of lupus[30]. Additionally, GLP-1RAs tend to stimulate the AMP-activated protein kinase pathway, which in turn will modulate stress and shift the intracellular macrophages to the M2 subtype while decreasing the M1 subtype in the bloodstream[30-32]. Th1 and Th17 cells are the primary lymphocytes driving autoimmune disturbances. GLP-1RA molecules inhibit their differentiation, thus blocking the cascade[30]. This dual effect of reducing pro-inflammatory immune responses while promoting regulatory mechanisms demonstrates the immunomodulatory potential of GLP-1RAs as one of the disease-modifying agents in treating chronic autoimmune conditions.

Unaffected by the immune regulation, the latter improves the shearing stress imposed on the endothelial cells by reducing the generation of reactive oxygen species and increasing the availability of nitric oxide, which is an important characteristic that will decrease the morbidity and mortality due to cardiovascular dysfunction in lupus patients[29,33].

GLP-1RA: POTENTIAL THERAPEUTIC BENEFITS FOR PSORIATIC ARTHRITITS

Psoriasis is an immune-driven condition that affects approximately 125 million people globally and is characterized by skin inflammation and associated systemic health problems[34]. About one-third of those with psoriasis go on to develop psoriatic arthritis (PsA), a chronic autoimmune disease presenting with a range of symptoms, such as enthesitis, dactylitis, axial disease, peripheral arthritis, nail problems, and psoriatic skin[35]. Individuals with PsA are more likely to be obese compared to those with RA, psoriasis, and the general population[36]. Studies have shown that an increased body mass index is associated with a higher risk of developing psoriasis and PsA[37]. Data suggest that obesity can trigger numerous immune-inflammatory pathways associated with PsA development. Addressing the link between obesity and PsA offers an opportunity to reduce PsA prevalence and improve its management by promoting weight loss, a modifiable risk factor[38].

Patients with PsA exhibit a higher prevalence of type 2 diabetes mellitus than the general population. The underlying mechanisms linking PsA to diabetes are complex and not yet fully understood[39]. In PsA, T cells are pivotal, showing elevated expression of Toll-like receptor 2 (but not Toll-like receptor 4) and a dominant Th1 and Th17 cell response[40]. Consequently, there is increased production of cytokines derived from T cells, such as TNF-α, IFN-γ, IL-2, IL-17, and granulocyte-macrophage colony-stimulating factor, in the synovial fluid, leading to joint inflammation[40].

The immune-modulating actions of GLP-1RAs suggest that these medications could offer therapeutic benefits for individuals with PsA, targeting both metabolic disturbances and inflammatory pathways characteristic of the disease[41]. Research indicates that GLP-1RAs can decrease the expression of pro-inflammatory cytokines like TNF-α, which plays a pivotal role in PsA pathogenesis. TNF-α enhances inflammation *via* the pro-survival transcription factor NF-κB, and GLP-1RAs have been shown to inhibit NF-κB activation[6]. However, while these findings are promising, the potential use of GLP-1RAs in PsA should not be based solely on their anti-inflammatory properties. Inflammation is a common feature of many diseases, and not all anti-inflammatory agents are effective treatments for PsA. Therefore, the therapeutic role of GLP-1RAs in PsA should be supported by condition-specific mechanistic studies and validated through targeted clinical trials.

DRUG-DRUG INTERACTIONS BETWEEN GLP-1RAS AND OTHER DRUGS

GLP-1RAs can affect concurrently administered drugs' pharmacokinetics (PK), primarily through their effects on gastrointestinal motility. The impact of these agents on the PK of drugs from different classes according to the Biopharmaceutics Classification System (BCS) has been studied[42]. For drugs in BCS Class I (high solubility, high permeability), such as warfarin and oral contraceptives[43], co-administration with GLP-1RAs resulted in delayed time to maximum concentration (t_{max}) and reduced maximum concentration (C_{max}). However, these changes were minor and not clinically significant, meaning no dose adjustments are necessary for these drugs when used alongside GLP-1RAs. Similar findings were reported when administering GLP-1RAs with drugs from BCS class II (low solubility, high permeability) such as statins[44], tacrolimus[45] and other medications from class III (high solubility, low permeability) such as angiotensin-converting enzyme inhibitors[46] as no significant changes in C_{max}, t_{max}, and area under the curve were reported.

Finally, when dealing with drugs from BCS Class IV (low solubility, low permeability) such as digoxin and erythromycin, certain considerations must be taken into account. Regarding digoxin, similar PK findings were reported as GLP-1RAs decrease its t_{max} and C_{max}[47,48], in addition to decreased area under the curve reported only with liraglutide [49]. Yet, the concentration of digoxin remained within its therapeutic range with no need for dosage adjustment. However, due to its narrow therapeutic range, it is recommended to monitor the concentration of digoxin at least during the first period of co-administration of the GLP-1RAs. As for erythromycin, it's important to consider its pharmacodynamic interaction with GLP-1RAs, as erythromycin counteracts GLP-1RAs' effect on delaying gastric emptying and reduces its postprandial antihyperglycemic effect[50].

Table 1 Summary of glucagon-like peptide-1 and its receptor agonist(s) benefits across rheumatic diseases

Disease	Pathophysiology	Mechanism of action of GLP-1RAs	Key outcomes	Evidence type
OA	Cartilage degradation, synovial inflammation, obesity-related inflammation	↓ MMPs and TNF-mediated catabolic enzymes. ↓ Synovial inflammation. Weight reduction	Delayed cartilage degradation. Improved joint integrity. Reduced pain and stiffness	Preclinical (*in vitro*/animal)
RA	Autoimmune synovial inflammation, joint erosion	↓ NF-κB signaling. ↓ Pro-inflammatory cytokines (TNF-α, IL-6, IL-1β). ↑ Treg activity	Reduced synovial inflammation. Reduced bone erosion. Improved immune regulation	Preclinical, limited clinical evidence
PsA	Inflammatory arthritis with metabolic syndrome involvement	↓ Th17/Th1 inflammatory pathways. ↓ Pro-inflammatory cytokines. Metabolic improvements (weight loss)	Decreased systemic inflammation. Potential joint protection. Improved metabolic comorbidities	Preclinical, limited clinical data
SLE	Autoantibody production, systemic inflammation	↓ Autoantibody production. ↓ Oxidative stress. Improved endothelial function	Reduced disease activity. Improved vascular outcomes	Preclinical (animal models), limited clinical
Common mechanisms	Chronic inflammation, metabolic dysregulation	↓ NF-κB signaling. ↑ cAMP leading to anti-inflammatory downstream effects. M2 macrophage polarization. Weight reduction	Reduced inflammatory burden. Improved metabolic profile	Preclinical and clinical (metabolic studies)

cAMP: Cyclic adenosine monophosphate; GLP-1RA: Glucagon-like peptide-1 and its receptor agonist(s); IL: Interleukin; MMP: Matrix metallopeptidase; NF-κB: Nuclear factor kappa B; OA: Osteoarthritis; PsA: Psoriatic arthritis; RA: Rheumatoid arthritis; SLE: Systemic lupus erythematosus; Th: T helper type; TNF-α: Tumor necrosis factor alpha.

SAFETY

Recent studies have been focusing on the safety profile of GLP-1RAs and their effect on various physiological systems.

Acute pancreatitis

Several cases of acute pancreatitis have been reported in both animal and human models treated with GLP-1RAs. However, the results were inconclusive, as studies reported varying effects on the pancreas, ranging from damage to no effect, to even possible improvements. Yet, additional cases of pancreatitis were documented after exenatide became available as a twice-daily treatment, which led the Food and Drug Administration to warn about potential drug-induced pancreatitis and the importance of monitoring for signs of pancreatitis in patients placed on these agents[51].

Medullary thyroid cancer

GLP-1RAs were associated with increased risk of medullary thyroid carcinoma in mice but not human models. This might be due to increased concentration of GLP-1RAs in mice, which favors cellular hyperplasia and subsequent carcinoma. Clinical studies, as well as surveillance post-marketing for these drugs, showed no association between these drugs and the incidence of medullary thyroid cancer[52]. Currently, no required monitoring for this cancer is recommended by the United States Food and Drug Administration[53]. However, it is important to note that all GLP-1RAs, except exenatide administered twice daily, are prohibited in patients with a personal or family history of medullary thyroid carcinoma as well as multiple endocrine neoplasia syndrome type 2.

Renal impairment

GLP-1RAs were found to be associated with acute kidney injury. For instance, several cases of altered kidney function were reported after the administration of exenatide twice daily. However, several factors influenced the results as patients were also predisposed to many factors that increase the risk of kidney injury, such as non-steroidal anti-inflammatory drugs use, hypertension, urinary tract infections, and other factors[53]. It is also important to note that decreased fluid intake and fluid loss that might result from nausea and vomiting, the main adverse effects of these agents, can further injure the kidneys. Among the GLP-1RAs, exenatide poses the highest risk since the kidneys eliminate it. Therefore, this drug, when given twice daily or once weekly, should be avoided in patients with creatinine clearance < 30 mL/minute or end-stage renal disease[53]. Regarding other GLP-1RAs, such as liraglutide and albiglutide, no dose adjustment is necessary in patients with renal impairment, as these drugs are not renally excreted. Yet, few cases of kidney injury were reported in patients with a history of moderate to severe renal impairment.

CONCLUSION

Initially, GLP-1RAs were designed for the treatment of metabolic disorders such as type 2 diabetes and obesity, new data suggest that these drugs tend to also express anti-inflammatory characteristics by modulation and down-regulating the immune response driven by the body. Current evidence points to their capacity to improve the biochemical indicators of metabolism and the chronic inflammatory state (Table 1). These drugs tend to be well tolerated by the patients, apart

from the mild gastrointestinal symptoms. However, patients with a history of renal insufficiency or a prior episode of acute pancreatitis should be monitored carefully. There is limited data on drug-drug interactions, however, patients on drugs that affect motility or those on pharmaceuticals that have a narrow therapeutic window require careful oversight.

FOOTNOTES

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REFERENCES

1 **Müller TD**, Finan B, Bloom SR, D'Alessio D, Drucker DJ, Flatt PR, Fritsche A, Gribble F, Grill HJ, Habener JF, Holst JJ, Langhans W, Meier JJ, Nauck MA, Perez-Tilve D, Pocai A, Reimann F, Sandoval DA, Schwartz TW, Seeley RJ, Stemmer K, Tang-Christensen M, Woods SC, DiMarchi RD, Tschöp MH. Glucagon-like peptide 1 (GLP-1). *Mol Metab* 2019; **30**: 72-130 [*RCA*] [PMID: 31767182 DOI: 10.1016/j.molmet.2019.09.010] [FullText] [Full Text(PDF)]

2 **Dailey MJ**, Moran TH. Glucagon-like peptide 1 and appetite. *Trends Endocrinol Metab* 2013; **24**: 85-91 [*RCA*] [PMID: 23332584 DOI: 10.1016/j.tem.2012.11.008] [FullText]

3 **Brunton S**. GLP-1 receptor agonists vs. DPP-4 inhibitors for type 2 diabetes: is one approach more successful or preferable than the other? *Int J Clin Pract* 2014; **68**: 557-567 [*RCA*] [PMID: 24499291 DOI: 10.1111/ijcp.12361] [FullText] [Full Text(PDF)]

4 **Graaf Cd**, Donnelly D, Wootten D, Lau J, Sexton PM, Miller LJ, Ahn JM, Liao J, Fletcher MM, Yang D, Brown AJ, Zhou C, Deng J, Wang MW. Glucagon-Like Peptide-1 and Its Class B G Protein-Coupled Receptors: A Long March to Therapeutic Successes. *Pharmacol Rev* 2016; **68**: 954-1013 [*RCA*] [PMID: 27630114 DOI: 10.1124/pr.115.011395] [FullText] [Full Text(PDF)]

5 **Hogan AE**, Tobin AM, Ahern T, Corrigan MA, Gaoatswe G, Jackson R, O'Reilly V, Lynch L, Doherty DG, Moynagh PN, Kirby B, O'Connell J, O'Shea D. Glucagon-like peptide-1 (GLP-1) and the regulation of human invariant natural killer T cells: lessons from obesity, diabetes and psoriasis. *Diabetologia* 2011; **54**: 2745-2754 [*RCA*] [PMID: 21744074 DOI: 10.1007/s00125-011-2232-3] [FullText] [Full Text(PDF)]

6 **Lee YS**, Jun HS. Anti-Inflammatory Effects of GLP-1-Based Therapies beyond Glucose Control. *Mediators Inflamm* 2016; **2016**: 3094642 [*RCA*] [PMID: 27110066 DOI: 10.1155/2016/3094642] [FullText] [Full Text(PDF)]

7 **Sen R**, Hurley JA. Osteoarthritis. 2023 Feb 20. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [PMID: 29493951] [FullText]

8 **Veronese N**, Cooper C, Reginster JY, Hochberg M, Branco J, Bruyère O, Chapurlat R, Al-Daghri N, Dennison E, Herrero-Beaumont G, Kaux JF, Maheu E, Rizzoli R, Roth R, Rovati LC, Uebelhart D, Vlaskovska M, Scheen A. Type 2 diabetes mellitus and osteoarthritis. *Semin Arthritis Rheum* 2019; **49**: 9-19 [*RCA*] [PMID: 30712918 DOI: 10.1016/j.semarthrit.2019.01.005] [FullText]

9 **Moore PW**, Malone K, VanValkenburg D, Rando LL, Williams BC, Matejowsky HG, Ahmadzadeh S, Shekoohi S, Cornett EM, Kaye AD. GLP-1 Agonists for Weight Loss: Pharmacology and Clinical Implications. *Adv Ther* 2023; **40**: 723-742 [*RCA*] [PMID: 36566341 DOI: 10.1007/s12325-022-02394-w] [FullText]

10 **Chen J**, Xie JJ, Shi KS, Gu YT, Wu CC, Xuan J, Ren Y, Chen L, Wu YS, Zhang XL, Xiao J, Wang DZ, Wang XY. Glucagon-like peptide-1 receptor regulates endoplasmic reticulum stress-induced apoptosis and the associated inflammatory response in chondrocytes and the progression of osteoarthritis in rat. *Cell Death Dis* 2018; **9**: 212 [*RCA*] [PMID: 29434185 DOI: 10.1038/s41419-017-0217-y] [FullText] [Full Text(PDF)]

11 **Wen ZQ**, Lin J, Xie WQ, Shan YH, Zhen GH, Li YS. Insights into the underlying pathogenesis and therapeutic potential of endoplasmic reticulum stress in degenerative musculoskeletal diseases. *Mil Med Res* 2023; **10**: 54 [*RCA*] [PMID: 37941072 DOI: 10.1186/s40779-023-00485-5] [FullText] [Full Text(PDF)]

12 **Mei J**, Sun J, Wu J, Zheng X. Liraglutide suppresses TNF-α-induced degradation of extracellular matrix in human chondrocytes: a therapeutic implication in osteoarthritis. *Am J Transl Res* 2019; **11**: 4800-4808 [*RCA*] [PMID: 31497200] [FullText]

13 **Meurot C**, Martin C, Sudre L, Breton J, Bougault C, Rattenbach R, Bismuth K, Jacques C, Berenbaum F. Liraglutide, a glucagon-like peptide 1 receptor agonist, exerts analgesic, anti-inflammatory and anti-degradative actions in osteoarthritis. *Sci Rep* 2022; **12**: 1567 [*RCA*] [PMID: 35091584 DOI: 10.1038/s41598-022-05323-7] [FullText] [Full Text(PDF)]

14 **Que Q**, Guo X, Zhan L, Chen S, Zhang Z, Ni X, Ye B, Wan S. The GLP-1 agonist, liraglutide, ameliorates inflammation through the activation of the PKA/CREB pathway in a rat model of knee osteoarthritis. *J Inflamm (Lond)* 2019; **16**: 13 [*RCA*] [PMID: 31182934 DOI:

10.1186/s12950-019-0218-y] [FullText] [Full Text(PDF)]

15 **Kosinska MK**, Ludwig TE, Liebisch G, Zhang R, Siebert HC, Wilhelm J, Kaesser U, Dettmeyer RB, Klein H, Ishaque B, Rickert M, Schmitz G, Schmidt TA, Steinmeyer J. Articular Joint Lubricants during Osteoarthritis and Rheumatoid Arthritis Display Altered Levels and Molecular Species. *PLoS One* 2015; **10**: e0125192 [*RCA*] [PMID: 25933137 DOI: 10.1371/journal.pone.0125192] [FullText] [Full Text(PDF)]

16 **Smolen JS**, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet* 2016; **388**: 2023-2038 [*RCA*] [PMID: 27156434 DOI: 10.1016/S0140-6736(16)30173-8] [FullText]

17 **Weyand CM**, Goronzy JJ. The immunology of rheumatoid arthritis. *Nat Immunol* 2021; **22**: 10-18 [*RCA*] [PMID: 33257900 DOI: 10.1038/s41590-020-00816-x] [FullText]

18 **McInnes IB**, Schett G. Pathogenetic insights from the treatment of rheumatoid arthritis. *Lancet* 2017; **389**: 2328-2337 [*RCA*] [PMID: 28612747 DOI: 10.1016/S0140-6736(17)31472-1] [FullText]

19 **Tao Y**, Ge G, Wang Q, Wang W, Zhang W, Bai J, Lin J, Shen J, Guo X, Xu Y, Geng D. Exenatide ameliorates inflammatory response in human rheumatoid arthritis fibroblast-like synoviocytes. *IUBMB Life* 2019; **71**: 969-977 [*RCA*] [PMID: 30897288 DOI: 10.1002/iub.2031] [FullText]

20 **Malemud CJ**. Matrix Metalloproteinases and Synovial Joint Pathology. *Prog Mol Biol Transl Sci* 2017; **148**: 305-325 [*RCA*] [PMID: 28662824 DOI: 10.1016/bs.pmbts.2017.03.003] [FullText]

21 **Mehdi SF**, Pusapati S, Anwar MS, Lohana D, Kumar P, Nandula SA, Nawaz FK, Tracey K, Yang H, LeRoith D, Brownstein MJ, Roth J. Glucagon-like peptide-1: a multi-faceted anti-inflammatory agent. *Front Immunol* 2023; **14**: 1148209 [*RCA*] [PMID: 37266425 DOI: 10.3389/fimmu.2023.1148209] [FullText] [Full Text(PDF)]

22 **Chiou HC**, Lin MW, Hsiao PJ, Chen CL, Chiao S, Lin TY, Chen YC, Wu DC, Lin MH. Dulaglutide Modulates the Development of Tissue-Infiltrating Th1/Th17 Cells and the Pathogenicity of Encephalitogenic Th1 Cells in the Central Nervous System. *Int J Mol Sci* 2019; **20**: 1584 [*RCA*] [PMID: 30934882 DOI: 10.3390/ijms20071584] [FullText] [Full Text(PDF)]

23 **McHugh J**. Rheumatoid arthritis: IFNγ drives synovial tissue remodelling. *Nat Rev Rheumatol* 2018; **14**: 63 [*RCA*] [PMID: 29323347 DOI: 10.1038/nrrheum.2017.221] [FullText]

24 **Gaffen SL**. The role of interleukin-17 in the pathogenesis of rheumatoid arthritis. *Curr Rheumatol Rep* 2009; **11**: 365-370 [*RCA*] [PMID: 19772832 DOI: 10.1007/s11926-009-0052-y] [FullText]

25 **Fortuna G**, Brennan MT. Systemic lupus erythematosus: epidemiology, pathophysiology, manifestations, and management. *Dent Clin North Am* 2013; **57**: 631-655 [*RCA*] [PMID: 24034070 DOI: 10.1016/j.cden.2013.06.003] [FullText]

26 **Pan L**, Lu MP, Wang JH, Xu M, Yang SR. Immunological pathogenesis and treatment of systemic lupus erythematosus. *World J Pediatr* 2020; **16**: 19-30 [*RCA*] [PMID: 30796732 DOI: 10.1007/s12519-019-00229-3] [FullText] [Full Text(PDF)]

27 **Nassar M**, Nassar O, Abosheaishaa H, Misra A. Comparative outcomes of systemic diseases in people with type 2 diabetes, or obesity alone treated with and without GLP-1 receptor agonists: a retrospective cohort study from the Global Collaborative Network : Author list. *J Endocrinol Invest* 2025; **48**: 483-497 [*RCA*] [PMID: 39302577 DOI: 10.1007/s40618-024-02466-4] [FullText]

28 **Karacabeyli D**, Lacaille D. Glucagon-Like Peptide 1 Receptor Agonists in Patients With Inflammatory Arthritis or Psoriasis: A Scoping Review. *J Clin Rheumatol* 2024; **30**: 26-31 [*RCA*] [PMID: 36870080 DOI: 10.1097/RHU.0000000000001949] [FullText]

29 **Noguchi T**, Katoh H, Nomura S, Okada K, Watanabe M. The GLP-1 receptor agonist exenatide improves recovery from spinal cord injury by inducing macrophage polarization toward the M2 phenotype. *Front Neurosci* 2024; **18**: 1342944 [*RCA*] [PMID: 38426018 DOI: 10.3389/fnins.2024.1342944] [FullText]

30 **Bendotti G**, Montefusco L, Lunati ME, Usuelli V, Pastore I, Lazzaroni E, Assi E, Seelam AJ, El Essawy B, Jang J, Loretelli C, D'Addio F, Berra C, Ben Nasr M, Zuccotti G, Fiorina P. The anti-inflammatory and immunological properties of GLP-1 Receptor Agonists. *Pharmacol Res* 2022; **182**: 106320 [*RCA*] [PMID: 35738455 DOI: 10.1016/j.phrs.2022.106320] [FullText]

31 **Wójcik P**, Gęgotek A, Žarković N, Skrzydlewska E. Oxidative Stress and Lipid Mediators Modulate Immune Cell Functions in Autoimmune Diseases. *Int J Mol Sci* 2021; **22**: 723 [*RCA*] [PMID: 33450863 DOI: 10.3390/ijms22020723] [FullText] [Full Text(PDF)]

32 **Armstrong AW**, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. *JAMA* 2020; **323**: 1945-1960 [*RCA*] [PMID: 32427307 DOI: 10.1001/jama.2020.4006] [FullText]

33 **McGonagle D**, Hermann KG, Tan AL. Differentiation between osteoarthritis and psoriatic arthritis: implications for pathogenesis and treatment in the biologic therapy era. *Rheumatology (Oxford)* 2015; **54**: 29-38 [*RCA*] [PMID: 25231177 DOI: 10.1093/rheumatology/keu328] [FullText]

34 **Bhole VM**, Choi HK, Burns LC, Vera Kellet C, Lacaille DV, Gladman DD, Dutz JP. Differences in body mass index among individuals with PsA, psoriasis, RA and the general population. *Rheumatology (Oxford)* 2012; **51**: 552-556 [*RCA*] [PMID: 22120603 DOI: 10.1093/rheumatology/ker349] [FullText]

35 **Aune D**, Snekvik I, Schlesinger S, Norat T, Riboli E, Vatten LJ. Body mass index, abdominal fatness, weight gain and the risk of psoriasis: a systematic review and dose-response meta-analysis of prospective studies. *Eur J Epidemiol* 2018; **33**: 1163-1178 [*RCA*] [PMID: 29680995 DOI: 10.1007/s10654-018-0366-z] [FullText] [Full Text(PDF)]

36 **Singh S**, Facciorusso A, Singh AG, Vande Casteele N, Zarrinpar A, Prokop LJ, Grunvald EL, Curtis JR, Sandborn WJ. Obesity and response to anti-tumor necrosis factor-α agents in patients with select immune-mediated inflammatory diseases: A systematic review and meta-analysis. *PLoS One* 2018; **13**: e0195123 [*RCA*] [PMID: 29771924 DOI: 10.1371/journal.pone.0195123] [FullText] [Full Text(PDF)]

37 **Wan MT**, Shin DB, Hubbard RA, Noe MH, Mehta NN, Gelfand JM. Psoriasis and the risk of diabetes: A prospective population-based cohort study. *J Am Acad Dermatol* 2018; **78**: 315-322.e1 [*RCA*] [PMID: 29128465 DOI: 10.1016/j.jaad.2017.10.050] [FullText]

38 **Nanus DE**, Filer AD, Hughes B, Fisher BA, Taylor PC, Stewart PM, Buckley CD, McInnes I, Cooper MS, Raza K. TNFα regulates cortisol metabolism in vivo in patients with inflammatory arthritis. *Ann Rheum Dis* 2015; **74**: 464-469 [*RCA*] [PMID: 24385202 DOI: 10.1136/annrheumdis-2013-203926] [FullText]

39 **Brunton SA**, Wysham CH. GLP-1 receptor agonists in the treatment of type 2 diabetes: role and clinical experience to date. *Postgrad Med* 2020; **132**: 3-14 [*RCA*] [PMID: 32815454 DOI: 10.1080/00325481.2020.1798099] [FullText]

40 **Calvarysky B**, Dotan I, Shepshelovich D, Leader A, Cohen TD. Drug-Drug Interactions Between Glucagon-Like Peptide 1 Receptor Agonists and Oral Medications: A Systematic Review. *Drug Saf* 2024; **47**: 439-451 [*RCA*] [PMID: 38273155 DOI: 10.1007/s40264-023-01392-3] [Full Text]

41 **Bush M**, Scott R, Watanalumlerd P, Zhi H, Lewis E. Effects of multiple doses of albiglutide on the pharmacokinetics, pharmacodynamics, and safety of digoxin, warfarin, or a low-dose oral contraceptive. *Postgrad Med* 2012; **124**: 55-72 [*RCA*] [PMID: 23322139 DOI:

10.3810/pgm.2012.11.2613] [FullText]

42 **Kothare PA**, Linnebjerg H, Skrivanek Z, Reddy S, Mace K, Pena A, Han J, Fineman M, Mitchell M. Exenatide effects on statin pharmacokinetics and lipid response. *Int J Clin Pharmacol Ther* 2007; **45**: 114-120 [*RCA*] [PMID: 17323791 DOI: 10.5414/cpp45114] [Full Text]

43 **Kothare PA**, Seger ME, Northrup J, Mace K, Mitchell MI, Linnebjerg H. Effect of exenatide on the pharmacokinetics of a combination oral contraceptive in healthy women: an open-label, randomised, crossover trial. *BMC Clin Pharmacol* 2012; **12**: 8 [*RCA*] [PMID: 22429273 DOI: 10.1186/1472-6904-12-8] [FullText] [Full Text(PDF)]

44 **Linnebjerg H**, Kothare P, Park S, Mace K, Mitchell M. The effect of exenatide on lisinopril pharmacodynamics and pharmacokinetics in patients with hypertension. *Int J Clin Pharmacol Ther* 2009; **47**: 651-658 [*RCA*] [PMID: 19840529 DOI: 10.5414/cpp47651] [FullText]

45 **Pinelli NR**, Patel A, Salinitri FD. Coadministration of liraglutide with tacrolimus in kidney transplant recipients: a case series. *Diabetes Care* 2013; **36**: e171-e172 [*RCA*] [PMID: 24065848 DOI: 10.2337/dc13-1066] [FullText] [Full Text(PDF)]

46 **de la Peña A**, Cui X, Geiser J, Loghin C. No Dose Adjustment is Recommended for Digoxin, Warfarin, Atorvastatin or a Combination Oral Contraceptive When Coadministered with Dulaglutide. *Clin Pharmacokinet* 2017; **56**: 1415-1427 [*RCA*] [PMID: 28357715 DOI: 10.1007/s40262-017-0531-7] [FullText]

47 **Kothare PA**, Soon DK, Linnebjerg H, Park S, Chan C, Yeo A, Lim M, Mace KF, Wise SD. Effect of exenatide on the steady-state pharmacokinetics of digoxin. *J Clin Pharmacol* 2005; **45**: 1032-1037 [*RCA*] [PMID: 16100297 DOI: 10.1177/0091270005278806] [FullText]

48 **Meier JJ**, Kemmeries G, Holst JJ, Nauck MA. Erythromycin antagonizes the deceleration of gastric emptying by glucagon-like peptide 1 and unmasks its insulinotropic effect in healthy subjects. *Diabetes* 2005; **54**: 2212-2218 [*RCA*] [PMID: 15983224 DOI: 10.2337/diabetes.54.7.2212] [FullText]

49 **Mundil D**, Cameron-Vendrig A, Husain M. GLP-1 receptor agonists: a clinical perspective on cardiovascular effects. *Diab Vasc Dis Res* 2012; **9**: 95-108 [*RCA*] [PMID: 22496442 DOI: 10.1177/1479164112441526] [FullText]

50 **Cefalu WT**, Buse JB, Del Prato S, Home PD, LeRoith D, Nauck MA, Raz I, Rosenstock J, Riddle MC. Beyond metformin: safety considerations in the decision-making process for selecting a second medication for type 2 diabetes management: reflections from a diabetes care editors' expert forum. *Diabetes Care* 2014; **37**: 2647-2659 [*RCA*] [PMID: 25147257 DOI: 10.2337/dc14-1395] [FullText] [Full Text (PDF)]

51 **United States Food and Drug Administration**. Guidance for industry diabetes mellitus – evaluating cardiovascular risk in new antidiabetic therapies to treat type 2 diabetes. [cited 9 July 2025]. Available from: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm071627.pdf

52 **Leiter LA**, Carr MC, Stewart M, Jones-Leone A, Scott R, Yang F, Handelsman Y. Efficacy and safety of the once-weekly GLP-1 receptor agonist albiglutide versus sitagliptin in patients with type 2 diabetes and renal impairment: a randomized phase III study. *Diabetes Care* 2014; **37**: 2723-2730 [*RCA*] [PMID: 25048383 DOI: 10.2337/dc13-2855] [FullText]

53 **Nordisk N**. Victoza® (liraglutide) injection 1.2 mg or 1.8 mg prescribing information. [cited 9 July 2025]. Available from: https://www.novo-pi.com/victoza.pdf

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