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Review Article

Natural Polymers for Buccal Adhesive Tablet Formulations: A Comprehensive Review

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Buccal drug delivery systems have gained substantial clinical significance due to their unique capacity to bypass hepatic first-pass metabolism, protect susceptible therapeutics from enzymatic degradation within the gastrointestinal tract, and provide sustained release patterns. Among the varied dosage forms utilized for this route, mucoadhesive buccal tablets represent a highly stable and versatile configuration. Traditionally, synthetic or semi-synthetic polymers have dominated the formulation landscape; however, modern pharmaceutical research has witnessed a paradigm shift toward natural polymers due to their superior biocompatibility, low toxicity, biodegradability, cost-effectiveness, and extensive structural abundance. This review paper comprehensively examines the functional roles of various natural polysaccharides and proteins, including chitosan, sodium alginate, pectin, xanthan gum, guar gum, gellan gum, and locust bean gum, in the design of buccal adhesive tablets. The fundamental physiological mechanisms governing mucoadhesion—spanning initial wetting, interpenetration, and mechanical interlocking with the mucus layer—are critically discussed. Furthermore, this paper highlights critical in vitro and in vivo evaluation metrics, therapeutic applications, persistent formulation challenges, and future clinical perspectives of natural polymer-based matrix systems, serving as an advanced compendium for formulation scientists.

Keywords: Buccal drug delivery, Mucoadhesion, Natural polymers, Chitosan, Sodium alginate, Evaluation parameters.

INTRODUCTION

The systemic administration of therapeutic molecules via the oral mucosa has generated considerable industrial and scientific interest within contemporary biopharmaceutics. The human buccal cavity provides an extremely attractive microenvironment for drug absorption, characterized by a highly vascularized epithelial lining, immediate entry into the systemic circulation via the internal jugular vein, and avoidance of the harsh acidic or enzymatic conditions inherent to the gastric lumen. Over the past decades, solid matrix configurations designed to adhere specifically to the buccal mucosa have emerged as a dominant technological platform for delivering molecules prone to intensive hepatic extraction. [1] Historically, formulation scientists relied heavily upon synthetic polymers such as carbomers, polyacrylic acid derivatives, and various cellulose ethers to achieve the requisite bioadhesive forces. While these synthetic macromolecular networks exhibit robust mechanical strength and predictable swelling kinetic behavior, they are frequently associated with localized mucosal irritation, transient tissue dehydration, and complex chemical synthesis validation protocols. Consequently, the contemporary pharmaceutical sector is experiencing an accelerated transition toward natural macromolecular components extracted from plant, marine, and microbial sources. [2] Natural polymers offer exceptional advantages over their synthetic counterparts, predominantly because their chemical architectures closely mimic biological tissues, rendering them intrinsically non-toxic, hypoallergenic, and entirely biocompatible. Furthermore, their structural abundance in nature

provides a sustainable supply chain that significantly reduces overall raw material procurement costs during commercial scale-up activities. The inherent chemical versatility of natural polysaccharides enables tailored structural modifications to fine-tune crosslinking density, swelling parameters, and drug release profiles. [3] In the architecture of a buccal adhesive tablet, the primary functional requirement of the polymeric matrix is to establish a rapid and durable interface with the mucosal epithelium upon hydration. Natural hydrophilic polymers undergo controlled swelling upon contact with saliva, creating an interconnected gel layer that facilitates molecular diffusion while simultaneously maintaining physical contact with the underlying tissue. This review aims to systematically analyze the diverse array of natural polymers utilized in solid buccal dosage forms, exploring their structural properties, adhesion mechanics, evaluation methodologies, and prospective applications in modern therapeutics. [4]

2. Advantages of Buccal Drug Delivery

The primary advantage of administering pharmacological agents via the buccal mucosa lies in the circumvention of hepatic first-pass metabolism, which frequently inactivates a high percentage of orally ingested drugs. By directing the absorbed drug directly into the systemic venous system, lower therapeutic doses can be administered, thereby expanding the therapeutic index and reducing systemic side effects. This pathway is particularly useful for hydrophobic small molecules, cardiovascular agents, and opioid analgesics that suffer from poor oral bioavailability. [5] Additionally, the buccal route shields sensitive chemical moieties, such as therapeutic peptides, proteins, and oligonucleotide sequences, from the highly destructive degradation pathways active within the gastrointestinal tract. The gastric environment exhibits extreme pH values and aggressive proteolytic enzymes that rapidly denature proteinaceous drugs before absorption can occur. In contrast, the buccal cavity maintains a relatively stable and neutral pH environment with limited enzymatic diversity, providing a protective window for the absorption of biopharmaceuticals. [6] From a patient compliance perspective, buccal adhesive tablets offer a non-invasive, painless, and controlled method of therapeutic delivery that is highly acceptable to pediatric and geriatric populations who suffer from dysphagia. Unlike conventional liquid or immediate-release oral tablets that cause rapid fluctuations in plasma drug concentrations, a well-designed buccal tablet provides sustained, zero-order or first-order release kinetics over prolonged intervals. Furthermore, in the event of an unexpected adverse clinical reaction or localized toxicity, the dosage form can be immediately removed by the patient, offering a crucial safety benefit. [7] Furthermore, the localized retention achieved by mucoadhesive tablets allows for targeted therapeutic intervention within the oral cavity itself, making it highly effective for treating aphthous ulcers, oral candidiasis, lichen planus, and periodontitis. The continuous secretion of saliva typically washes away conventional gels, ointments, and mouthwashes within minutes, necessitating frequent reapplication. Buccal adhesive matrices resist this salivary clearance mechanism, ensuring that a concentrated dose of the active pharmaceutical ingredient remains in direct, uninterrupted contact with the lesion. [8]

3. Mechanism of Mucoadhesion

The phenomenon of mucoadhesion within the buccal cavity involves a complex sequence of physical and chemical interactions between the hydrated polymer chains of the tablet and the glycoprotein networks composing the mucus layer. The initial stage, frequently designated as the contact phase, occurs when the solid tablet is placed on the mucosal surface and undergoes wetting by the surrounding salivary fluid. This moisture absorption induces structural relaxation of the tightly coiled polymer matrices, leading to deep volumetric swelling and exposure of active functional groups. [9] Following the initial contact, the consolidation phase takes place, wherein the relaxed, mobile polymer chains physically interpenetrate and entangle with the highly branched oligosaccharide chains of mucin glycoproteins. This interdiffusion process requires that the polymer chains possess sufficient structural flexibility and appropriate molecular weight to overcome steric barriers presented by the biological matrix. The depth of chain interpenetration directly dictates the ultimate mechanical resistance of the bioadhesive interface against physiological shear stresses. [10] To quantify

and explain these multi-step phenomena, multiple theoretical models have been advanced, among which the electronic, adsorption, and diffusion theories are the most widely cited. The electronic theory proposes that the transfer of electrons across the polymer-mucus interface results in the formation of a double layer of electrical charge, generating attractive electrostatic forces. Conversely, the adsorption theory dictates that primary adhesion is driven by secondary chemical bonds, such as hydrogen bonding, van der Waals forces, and hydrophobic interactions, which occur between the hydroxyl or carboxyl groups of the polymer and the mucin segments. [11] The mechanical and fracture theories focus on the bulk properties of the system, evaluating the physical resistance required to rupture the adhesive bond after hydration has reached equilibrium. The fracture theory relates the adhesive strength directly to the cohesive forces within the swollen gel layer, asserting that bond failure typically occurs at the weakest plane within the interpenetrated network. Factors such as localized hydration rate, polymer crosslinking density, matrix flexibility, and contact pressure applied during placement collectively govern the failure kinetics of the matrix. [12]

4. Natural Polymers Used In Buccal Adhesive Tablets

Chitosan: A linear cationic polysaccharide derived from the partial deacetylation of chitin obtained from crustacean exoskeletons, remains one of the most widely investigated natural polymers for buccal applications. The primary amino groups distributed along its backbone impart a strong positive charge at physiological pH, allowing for intense electrostatic interactions with the negatively charged sialic acid and sulfonic acid residues of mucin molecules. Moreover, chitosan possesses well-documented permeation-enhancing properties, transiently opening the tight junctions of the epithelial barrier to facilitate paracellular drug transport. [13]

Sodium Alginate: A hydrophilic linear anionic polysaccharide isolated extensively from marine brown algae, comprising varying ratios of β-D-mannuronic acid and α-L-guluronic acid residues. Upon hydration in the buccal cavity, sodium alginate forms a highly viscous, cohesive gel layer capable of establishing extensive hydrogen-bonding networks with mucus proteins. Its excellent structural compatibility with divalent cations like calcium allows for controlled crosslinking, which can be strategically utilized to modify the matrix degradation rate and slow down the release of highly water-soluble drugs. [14]

Pectin: A structural heteropolysaccharide extracted predominantly from the cellular walls of citrus fruits and apple pomace, consists primarily of α-(1-4)-linked D-galacturonic acid units. The mucoadhesive capabilities of pectin are closely dictated by its degree of esterification, which influences its hydration rate, water-binding capacity, and structural chain flexibility. Low-methoxyl pectins form robust gels in the presence of salivary cations, rendering them exceptionally stable matrix-forming agents for buccal tablets that require prolonged delivery periods. [15]

Xanthan Gum: A high-molecular-weight extracellular heteropoly saccharide produced via the aerobic fermentation of glucose or sucrose by the bacterium Xanthomonas campestris. Its structural backbone is identical to cellulose, with trisaccharide side chains that provide exceptional thermal, chemical, and enzymatic stability across a wide range of pH conditions. When integrated into buccal formulations, xanthan gum exhibits excellent pseudo-plastic flow properties and rapid hydration kinetics, creating an elastic gel barrier that controls drug diffusion while resisting mechanical dislodgement during mastication and speech. [16]

Guar Gum: A non-ionic galactomannan derived from the endosperm of the seeds of Cyamopsis tetragonoloba, features a linear chain of D-mannose units with D-galactose branches. Due to its high abundance of hydroxyl groups, guar gum exhibits an exceptional water-binding capacity, facilitating rapid hydration and swelling even in environments with limited salivary volume. Because it is non-ionic, its mucoadhesive performance and matrix viscosity are remarkably stable against variations in salivary ionic strength or alterations in local pH. [17]

Gellan Gum: An anionic microbial exopolysaccharide generated by the fermentation of Sphingomonas elodea, forming a characteristic tetrasaccharide repeating unit. A unique attribute of

gellan gum is its capacity for in situ gelation, transitioning from a low-viscosity fluid to a firm, structurally rigid gel network upon interaction with the mono- and divalent cations naturally present in human saliva. This ion-activated restructuring significantly boosts the mechanical cohesive strength of the buccal tablet, preventing premature disintegration and ensuring a steady, prolonged drug release. [18]

Locust Bean Gum: Also known as carob gum, is another non-ionic galactomannan extracted from the seeds of the carob tree, Ceratonia siliqua. It exhibits limited cold-water solubility and requires synergy with other polysaccharides, such as xanthan gum or kappa-carrageenan, to form fully cohesive, crosslinked hydrogel networks. This synergistic blending is highly advantageous in buccal tablet formulation, as it allows developers to optimize matrix elasticity, minimize erosion rates, and achieve precise zero-order drug release profiles. [19]

Agarose and Carrageenan: Sourced from marine red seaweeds, are also being utilized due to their thermoreversible gelation profiles and high molecular weights. These sulfated polysaccharides interact with mucosal structures through strong hydrogen bonding and physical entanglement. By adjusting the ratios of these marine polymers within a compressed matrix, formulation scientists can manipulate the disintegration time of the tablet from one hour to over eight hours. [20]

Plant-Derived Mucilages: Such as those extracted from Isabgol (Plantago ovata) husks, Aloe vera leaves, and Hibiscus rosa-sinensis leaves, are gaining rapid traction as novel mucoadhesive excipients. These mucilages consist of complex mixtures of highly branched polysaccharides that exhibit rapid swelling profiles upon contact with moisture. Due to their high molecular weight and excellent biocompatibility, these green excipients represent an eco-friendly and cost-efficient alternative to conventional synthetic polymers. [21]

Starch and Derivatives: Including pregelatinized starch, carboxymethyl starch, and hydroxypropyl starch, serve as versatile matrix-forming agents in buccal compression protocols. While native starch possess poor mucoadhesive properties, chemical modification introduces functional carboxymethyl or hydroxypropyl groups that significantly increase hydrophilicity and molecular chain flexibility. These engineered starches combine excellent binding properties during dry compression with controllable swelling characteristics upon exposure to saliva. [22]

Proteins: In addition to polysaccharides, natural proteinaceous polymers such as gelatin, zein, and soy protein isolates are being investigated for specialized buccal delivery systems. Proteins possess unique amphiphilic structures and diverse amino acid side chains that can form both hydrophobic interactions and hydrogen bonds with mucin glycoproteins. Their rapid biodegradation profiles make them suitable for short-term buccal delivery applications, where rapid drug release paired with safe matrix dissolution is clinically desired. [23] The choice of a specific natural polymer or polymer blend must be guided by the physicochemical characteristics of the active pharmaceutical ingredient, including its water solubility, molecular size, and therapeutic dose. Hydrophilic molecules are rapidly released from highly porous polymer matrices, requiring dense, slow-eroding polymers like xanthan gum or crosslinked alginates to restrict diffusion. Conversely, poorly water-soluble drugs necessitate highly hydrophilic polymers that promote fast wetting and local solubilization within the microenvironment of the swelling tablet matrix. [24]

5. Evaluation Parameters

The rigorous characterization of buccal adhesive tablets requires a multi-faceted testing protocol encompassing physical, mechanical, and biological evaluations to guarantee performance, safety, and reproducibility. The initial phase of evaluation involves standard compendial tests, including thickness, diameter, weight variation, and hardness metrics, using standardized pharmaceutical testing equipment. Ensuring uniform hardness is crucial, as a tablet that is too soft will erode prematurely under salivary flow, while an overly compressed matrix may fail to hydrate adequately. [25]

Surface pH Determination: A critical quality control parameter performed to predict the potential for localized mucosal irritation after application. A highly acidic or alkaline matrix surface can provoke

inflammatory responses, tissue ulceration, and patient discomfort during prolonged contact. To evaluate this, tablets are allowed to swell in a limited volume of simulated salivary fluid, and the pH is measured at regular intervals using a calibrated micro-electrode placed in close proximity to the gel layer. [26]

Swelling Index and Water Uptake Kinetics: Evaluated to analyze the hydration dynamics of the hydrophilic natural polymers over time. Tablets are weighed initially in their dry state, placed into simulated saliva at physiological temperature, and periodically removed to record their wet weight after removing excess surface moisture. A highly rapid, uncontrolled swelling behavior can lead to a drastic loss of structural integrity, causing the tablet to transform into a fluid mass that is easily swallowed. [27]

Ex Vivo Mucoadhesive Strength: Traditionally quantified by measuring the maximum force required to detach the formulated tablet from a freshly excised layer of bovine, porcine, or caprine buccal mucosa. Modified texture analyzers or custom-designed tensile strength testers are utilized, where the mucosal tissue is secured and brought into contact with the tablet under a defined initial force for a specific duration. The peak force required to separate the interface is recorded as the mucoadhesive strength, providing a quantitative index of clinical retention. [28]

Ex Vivo Mucoadhesion Time: Determined using modified disintegration apparatuses or rotating cylinder methods to simulate the hydrodynamic shear stresses present within the human mouth. The mucosal tissue is glued onto a solid support, the tablet is adhered to it, and the entire assembly is immersed and agitated within simulated saliva. The time required for the tablet to completely detach from the mucosal surface or undergo total matrix erosion is visually monitored and recorded as the total mucoadhesion time. [29]

In Vitro Drug Release Profiles: Established using standard USP dissolution apparatuses (Type I or Type II) modified to simulate the restricted fluid volumes characteristic of the buccal cavity. Samples of the dissolution medium are withdrawn at predefined intervals and analyzed via UV-Visible spectroscopy or High-Performance Liquid Chromatography (HPLC) to map the cumulative drug release curve. Mathematical models, such as the Higuchi, Korsmeyer-Peppas, and zero-order equations, are subsequently applied to the dissolution data to determine whether drug transport is driven by pure Fickian diffusion, polymer erosion, or anomalous transport. [30]

Ex Vivo Permeation Studies: Executed using modified Franz diffusion cells to evaluate the trans-mucosal transport kinetics of the released drug across an excised buccal membrane layer. The mucosal tissue is carefully mounted between the donor and receptor compartments, with the donor compartment receiving the formulation in simulated saliva, while the receptor cell is filled with physiological buffer. Periodic sampling from the receptor chamber allows for the calculation of the steady-state flux, permeability coefficient, and lag time, indicating the prospective in vivo absorption profile. [31]

6. APPLICATIONS

Natural polymer-based buccal adhesive tablets have been extensively investigated for delivering cardiovascular drugs, such as beta-blockers, calcium channel antagonists, and nitrates, which typically exhibit poor oral bioavailability due to heavy first-pass hepatic extraction. Formulations utilizing sodium alginate and chitosan blends have successfully delivered carvedilol, nitrendipine, and isosorbide dinitrate over extended periods, maintaining stable plasma concentrations and minimizing acute hypertensive episodes. These systems ensure that therapeutic molecules enter the systemic circulation directly, optimizing efficacy while reducing dose-dependent toxicities. [32] Another major therapeutic application lies in emergency pain management and breakthrough pain control, where rapid clinical onset is essential. Buccal tablets containing fentanyl citrate or buprenorphine formulated with fast-swelling natural mucilages provide an immediate analgesic effect that mimics intravenous administration without its associated risks and clinical complexity. The rapid initial hydration of the natural polymers allows for immediate transmucosal transport, offering rapid relief to cancer patients experiencing sudden pain spikes. [33] The

delivery of hormone replacement therapies, including progesterone, testosterone, and estradiol, has also been revolutionized by the application of mucoadhesive buccal matrices. When swallowed conventionally, these steroidal hormones undergo rapid hepatic destruction, requiring high oral doses that increase the risk of hepatic tumors and thromboembolic disorders. Buccal administration via guar gum or pectin matrices achieves therapeutic systemic levels with a fraction of the oral dose, establishing a safer, more stable hormonal profile. [34] Furthermore, buccal adhesive tablets are uniquely suited for managing localized pathologies within the oral cavity, including severe oral candidiasis, recurring aphthous stomatitis, and aggressive periodontal disease. By immobilizing antifungal agents like miconazole or broad-spectrum antimicrobials like chlorhexidine within a slow-eroding xanthan gum matrix, the drug is released directly into the saliva over several hours. This sustained localized concentration eradicates pathogens far more effectively than conventional oral rinses, which are quickly cleared by salivation and swallowing. [35]

CHALLENGES AND LIMITATIONS

Despite the numerous advantages, the development of natural polymer-based buccal adhesive tablets faces several substantial challenges, primarily stemming from the inherent physiological properties of the oral cavity. The total surface area available for drug absorption within the buccal region is relatively constrained, typically estimated at only 50 square centimeters, which strictly limits the maximum drug dose that can be delivered. Consequently, this route is largely restricted to highly potent therapeutic agents that produce clinical effects at low milligram or microgram doses. [36] Another significant barrier is the continuous secretion of saliva, which can wash away the drug from the absorption site, a phenomenon known as the "salivary scavenging effect." Saliva production triggers involuntary swallowing, redirecting a portion of the released drug into the gastrointestinal tract and partially defeating the purpose of buccal administration. To counteract this, formulation scientists must develop asymmetric, bilayered tablets featuring an impermeable backing layer that forces unidirectional drug release toward the mucosa. [37] The variable permeability of the non-keratinized buccal epithelium presents a major obstacle to the transport of large, hydrophilic macromolecular therapies, including peptides and proteins. The intercellular lipid lamellae and tight junctions within the epithelial layer restrict paracellular transport, resulting in low bioavailability for high-molecular-weight drugs. While natural polymers like chitosan act as transient permeation enhancers, finding the optimal balance between enhancing absorption and preventing localized tissue toxicity remains a difficult formulation challenge. [38] Furthermore, natural polymers suffer from inherent batch-to-batch variability regarding molecular weight, purity, viscosity, and chemical composition, which are heavily influenced by geographic origin, harvesting seasons, and extraction techniques. This lack of standardization complicates regulatory compliance, as variations in polymer characteristics can directly alter tablet hardness, swelling kinetics, and drug release profiles. Overcoming these natural inconsistencies requires rigorous purification, comprehensive standardization, and advanced chemical characterization protocols. [39]

FUTURE PERSPECTIVES

The future of natural polymer-based buccal drug delivery lies in the strategic development of smart, stimuli-responsive hydrogel matrices and tailored chemical modifications. Thiolation of natural polysaccharides, which involves covalently attaching sulfhydryl groups to the polymer backbone, represents a major breakthrough that significantly enhances mucoadhesive strength through disulfide bond formation with mucin cysteines. These thiolated derivatives, such as thiolated chitosan or thiolated alginate, provide vastly superior retention times and enhanced permeation pathways compared to unmodified native polymers. [40] Another promising avenue is the integration of nanotechnology within mucoadhesive buccal systems, creating advanced nano-in-gel or nano-compressed tablet configurations. Nanoparticles, liposomes, or solid lipid nanoparticles loaded with poorly soluble drugs can be uniformly dispersed within a natural polymer matrix, combining the benefits of nano-sized dissolution enhancement with the prolonged retention

offered by the bioadhesive tablet. This hybrid approach holds great potential for the non-invasive systemic delivery of complex macromolecules, biomacromolecules, and personalized biological therapies. [41]

CONCLUSION

In conclusion, natural polymers represent an exceptional and highly adaptable material platform for fabricating advanced mucoadhesive buccal adhesive tablet formulations. Their unparalleled biocompatibility, structural diversity, non-toxic nature, and rich abundance make them highly attractive alternatives to traditional synthetic polymers. By undergoing controlled hydration and forming strong non-covalent or electrostatic bonds with the mucus layer, these biopolymers provide sustained, unidirectional therapeutic delivery that bypasses first-pass metabolism and protects sensitive drug molecules. While issues such as batch variability and restricted absorption areas persist, ongoing research into chemical modifications and nanotechnological integration will undoubtedly expand the clinical utility of these systems, cementing their role in future drug delivery paradigms. [42].

REFERENCES

1. Ajmal CS, Yerram S, Abishek V, Muhammed Nizam VP, Aglave G, Patnam JD, et al. Innovative approaches in regulatory affairs: Leveraging artificial intelligence and machine learning for efficient compliance and decisionmaking. AAPS J [Internet]. 2025 [cited 2026 Feb 18]; 27:22. Available from: doi:10.1208/s12248-02401002-w
2. Bishnoi M, Sonker A. Emergency use authorization of medicines: History and ethical dilemma. Perspect Clin Res [Internet]. 2023 [cited 2026 Feb 18];14(2):49-55. Available from: doi: 10.4103/picr.picr_149_22
3. Collier R, Singh A, Chopra S. Harnessing AI/ML in drug and biological products discovery and development: The regulatory perspective. Pharmaceuticals (Basel) [Internet]. 2025 [cited 2026 Feb 18];18(1):47. Available from: doi: 10.3390/ph18010047
4. Di Bello F, Russo E, Sartori M. Enhancing regulatory affairs in the market placing of new medical devices: How LLMs like ChatGPT may support regulatory processes. AboutOpen [Internet]. 2024 [cited 2026 Feb 18];11(1):7788. Available from: doi: 10.33393/ao.2024.3302
5. Dawar V, Sharma A, Mittal V, Sharma D. Global harmonization in drug approval: Bridging regulatory and clinical trial diversity. Curr Indian Sci [Internet]. 2024 [cited 2026 Feb 18];2(3).
6. Liu Q, Huang R, Hsieh J, Zhu H, Tiwari M, Liu G, et al. Landscape analysis of artificial intelligence and machine learning in regulatory submissions for drug development from 2016-2021. Clin Pharmacol Ther [Internet]. 2023 [cited 2026 Feb 18];113(4):771-4. Available from: doi:10.1002/cpt.2668
7. Niazi SK, Al-Shaqha WM, Mirza Z. Proposal of International Council for Harmonization guideline for approval of biosimilars. J Mark Access Health Policy [Internet]. 2022 [cited 2026 Feb 18];11(1). Available from: doi: 10.1080/20016689.2022.2147286
8. Pantanowitz L, Hanna M, Pantanowitz J, Lennerz J, Henricks WH, Shen P, et al. Regulatory aspects of artificial intelligence and machine learning. Arch Pathol Lab Med [Internet]. 2024 [cited 2026 Feb 18];148(10):1185-94. Available doi:10.5858/arpa.2023-0123-RA from:
9. Suresh V, Kumar KS. Approval and marketing of medical products in EU, USA, India and Australia. Asian J Med Pharm Sci [Internet]. 2023 [cited 2026 Feb 18];11(1):7382. Available from: doi: 10.30904/j.ajmps.2023.4619
10. Sireesha B, Haritha S, Lakshmi Thriveni S, Nikitha P, Vijaya Lakshmi UVS. Regulatory affairs and regulatory requirements for new drug approval. Int J Health Care Biol Sci [Internet]. 2024 [cited 2026 Feb 18];5(4):22-28. Available from: doi: 10.46795/ijhcbs. v5i4.643
11. Beninger P. Signal management in pharmacovigilance: A review of activities and case studies. Clin Ther [Internet]. 2020 [cited 2026 Feb 18];42(6):1110-29. Available from: doi: 10.1016/j.clinthera.2020.03.018
12. Craveiro NS, Lopes BS, Tomás L, Almeida SF. Drug withdrawal due to safety: A review supporting withdrawal decisions. Curr Drug Saf [Internet]. 2020 [cited 2026 Feb 18];15(1):4-12. Available from: doi:10.2174/1574886314666191004092520

13. Gozzo L. Pharmacovigilance and appropriate drug use. Healthcare [Internet]. 2024 [cited 2026 Feb 18]; 12(6):669. Available from: doi: 10.3390/healthcare12060669
14. Holm JEJ, Ruppert JG, Ramsden SD. Impact of changing regulations on lifecycle safety concerns. Pharm Med [Internet]. 2022 [cited 2026 Feb 18];36(1):33-46. Available from: doi:10.1007/s40290-021-00414-8
15. Kandukuri A, Edla DR. Ensuring data safety: Pharmacovigilance processes and ADR reporting systems. Asian J Pharm Res Dev [Internet]. 2025 [cited 2026 Feb 18];13(3):1569. Available from: doi:10.22270/ajprd. v13i3.1569
16. Khan MAA, Hamid S, Khan SA, Sarfraz M, Babar ZUD. Stakeholders views on pharmacovigilance policy coordination in Pakistan. Front Pharmacol [Internet]. 2022 [cited 2026 Feb 18]: 13:891954. Available from: doi: 10.3389/fphar.2022.891954
17. Kiguba R, Olsson S, Waitt C. Pharmacovigilance in low- and middle-income countries. Br J Clin Pharmacol [Internet]. 2023 [cited 2026 Feb 18];89(2):491-509. Available from: doi: 10.1111/bep.15193
18. Lucas S, Ailani J, Smith TR, Abdrabboh A, Xue F, Navetta MS. Pharmacovigilance reporting requirements throughout product lifecycle. Ther Adv Drug Saf [Internet]. 2022 [cited 2026 Feb 18];13. Available from: doi:10.1177/20420986221125006
19. Pozsgai K, Szűcs G, Kőnig-Péter A, Balázs O, Vajda P, Botz L, et al. Pharmacovigilance database analysis for ADRs related to falsified medical products. Front Pharmacol [Internet]. 2022 [cited 2026 Feb 18]; 13:964399. Available from: doi: 10.3389/fphar.2022.964399
20. Rewale KS, Tuwar AB, Salve MT. A brief review on pharmacovigilance. Int J Pharm Sci Drug Anal [Internet]. 2024 [cited 2026 Feb 18];4(1):9-16.
21. Robinson F, Wilkes S, Schaefer N, Goldstein M, Rice M, Gray J, et al. Patient-centered pharmacovigilance priority actions. Ther Adv Drug Saf [Internet]. 2023 [cited 2026 Feb 18]; 14. Available from: doi:10.1177/20420986221146418
22. Sardella M, Belcher G, Lungu C, Ignoni T, Camisa M, Stenver DI, et al. Monitoring manufacturing and quality of medicines in pharmacovigilance. Ther Adv Drug Saf [Internet]. 2021 [cited 2026 Feb 18];12. Available from: doi:10.1177/20420986211038436
23. Singh A, Kumar A. Pharmacovigilance in cell and gene therapy: Regulatory perspectives. Drug Saf [Internet]. 2025 [cited 2026 Feb 18]. Available from: doi: 10.1007/s40264-025-01596-9
24. CDSCO alerts: Retrospective dosage form-wise quality control analysis (2018-2023). Regul Toxicol Pharmacol [Internet]. 2025 [cited 2026 Feb 18]; 156:105775. Available from: doi: 10.1016/j.yrtph.2025.105775
25. Alemayehu C, Mitchell G, Nikles J. Barriers for conducting clinical trials in developing countries. Int J Equity Health [Internet]. 2018 [cited 2026 Feb 18]; 17:37. Available from: doi:10.1186/s12939-018-0748-6
26. Almutairi K, Nossent J, Preen D, Keen H, Inderjeeth C. Global prevalence of rheumatoid arthritis: Meta-analysis. Rheumatol Int [Internet]. 2021 [cited 2026 Feb 18];41(5):863-77. Available from: doi: 10.1007/s00296020-04731-0
27. Dirks A, Florez M, Torche F, Young S, Slizgi B, Getz K. Risk-based quality management adoption in clinical trials. Ther Innov Regul Sci [Internet]. 2024 [cited 2026 Feb 18]; 58:520-7. Available from: doi:10.1007/s43441- 02400618-5
28. Harrold LR, Bryson J, Lehman T, et al. Association between anti-CCP antibodies and clinical response in RA patients. Rheumatol Ther [Internet]. 2021 [cited 2026 Feb 18]; 8(2):937-53. Available from: doi: 10.1007/s40744- 02100310-2
29. International Council for Harmonisation. ICH E6(R3) Good Clinical Practice guideline [Internet]. Geneva: ICH; 2025 [cited 2026 Feb 18]. Available from: https://www.ich.org
30. Ridha A, Hussein S, AlJabban A, Gunay LM, Gorial FI, Al Ani NA. Clinical impact of seropositivity in rheumatoid arthritis treated with etanercept. Open Access Rheumatol [Internet]. 2022 [cited 2026 Feb 18] 14:113-21. Available from: doi:10.2147/OARRR.S368190
31. Maurya MR, Munshi R. Safety analysis of REMS for US FDA approved drugs. Indian J Med Res [Internet]. 2024 [cited 2026 Feb 18]; 159(6):581-4. Available from: doi:10.25259/ijmr_350 22
32. Youssef A, Hammad TA. Pharmacovigilance due diligence in drug development. Drug Saf

[Internet]. 2025 [cited 2026 Feb 18]. Available from: doi: 10.1007/s40264-025-01640-8
33. Harmark L, van Grootheest AC. Pharmacovigilance: Methods and future perspectives. Eur J Clin Pharmacol [Internet]. 2008 [cited 2026 Feb 18]:64(8):743-52. Available from: doi:10.1007/s00228-008-0475-9
34. Harmonizing health: Global analysis of pharmaceutical regulatory activities. PMC [Internet]. 2025 [cited 2026 Feb 18].
35. International Council for Harmonisation. ICH Q8-Q10 pharmaceutical quality guidelines [Internet]. Geneva: ICH; 2009 [cited 2026 Feb 18]. Available from: https://www.ich.org
36. International Council for Harmonisation. Common Technical Document M4 guideline [Internet]. Geneva: ICH; 2000 [cited 2026 Feb 18]. Available from: https://www.ich.org
37. Jeetu G, Anusha G. Pharmacovigilance: Worldwide master key for drug safety monitoring. J Young Pharm [Internet]. 2010 [cited 2026 Feb 18];2(3):315-20. Available from: doi:10.4103/0975-1483.66802
38. Leligkou HC, Gerogiannis VC. Deep transformers for ALCOA+ data integrity compliance. Appl Sci [Internet]. 2023 [cited 2026 Feb 18];13(13):7616. Available from: doi:10.3390/app13137616
39. Murali K, Kaur S, Prakash A, Medhi B. Artificial intelligence in pharmacovigilance: Practical utility. Indian J Pharmacol [Internet]. 2019 [cited 2026 Feb 18];51(6):373-6. Available from: doi: 10.4103/ijp.IJP_814_19
40. Rahman MS, Rahman MK, Kaykobad M, Rahman MS. Application of LIME and SHAP in Alzheimer's disease detection. Brain Inform [Internet]. 2024 [cited 2026 Feb 18];11(1):4. Available from: doi:10.1186/s40708-02400213-9
41. Santoro A, Genov G, Spooner A, Raine J, Arlett P. European Union pharmacovigilance system and public health protection. Drug Saf [Internet]. 2017 [cited 2026 Feb 18];40(10):855-69. Available from: doi:10.1007/s40264-017-0572-8
42. Silva MR, Santos LK, Oliveira PJ, et al. Artificial intelligence in Brazilian pharmaceutical regulation: Pilot program results. Regul Sci Med Prod [Internet]. 2024 [cited 2026 Feb 18]; 14:189-98.

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