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CONTROLLED RELEASE KINETICS OF 6-BENZYLAMINOPURINE DERIVATIVES FROM A HYDROGEL MATRIX

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Abstract: Controlled delivery of biologically active compounds is an essential requirement for modern regenerative veterinary materials. In this study, the release kinetics of 6-benzylaminopurine (BAP) derivatives from a biocompatible hydrogel matrix was investigated. The hydrogel carrier was prepared from natural polymer components using ionic crosslinking to obtain a three-dimensional porous network capable of retaining water and gradually releasing the active compound. The incorporation of BAP derivatives into the matrix was carried out during gel formation to achieve uniform distribution and prevent rapid diffusion from the wound surface.

Physicochemical characterization showed high swelling capacity and stable structural integrity of the hydrogel under physiological conditions. Release experiments performed in buffer medium at body temperature demonstrated a biphasic profile consisting of an initial moderate release followed by a prolonged diffusion-controlled stage. The release behavior corresponded to non-Fickian transport, indicating combined diffusion and polymer relaxation mechanisms. Mathematical modeling confirmed sustained liberation of BAP derivatives over an extended period, maintaining therapeutically relevant concentrations.

The obtained results suggest that immobilization of 6-benzylaminopurine derivatives in a hydrogel matrix provides controlled and prolonged delivery, which is beneficial for regenerative applications and reduction of repeated topical treatments in veterinary practice.

Keywords: 6-Benzylaminopurine; hydrogel matrix; controlled release; release kinetics; diffusion mechanism; regenerative biomaterials; veterinary applications.

Introduction

Sustained delivery of biologically active substances is a key requirement for the development of modern regenerative biomaterials used in veterinary medicine. In livestock production, skin injuries and inflammatory lesions frequently occur as a result of mechanical trauma, surgical procedures and environmental stress. Effective treatment requires not only antimicrobial protection but also stimulation of tissue regeneration. However, conventional topical preparations release active substances rapidly, resulting in short therapeutic action and the need for repeated application. Therefore, controlled drug-release systems capable of maintaining stable local concentrations are of particular interest.

Hydrogels represent one of the most promising carriers for local delivery of pharmacologically active compounds. These materials consist of three-dimensional hydrophilic polymer networks capable of absorbing large amounts of water while preserving structural integrity. Due to their high permeability to oxygen, flexibility and similarity to biological tissues, hydrogels provide a favorable environment for cell migration and tissue repair. Additionally, polymer matrices can regulate diffusion of incorporated molecules, enabling gradual and prolonged release directly at the target site. The release behavior depends on polymer composition, crosslinking density and interaction between the active compound and the matri[1-10].

6-Benzylaminopurine (BAP) and its derivatives belong to a group of purine-based biologically active compounds known for their regulatory influence on cellular metabolism and proliferation. Purine structures participate in nucleic acid synthesis and energy transfer processes, which are closely related to tissue regeneration mechanisms. When applied locally, BAP derivatives can stimulate fibroblast activity and formation of new tissue structures. Nevertheless, direct administration of low-molecular purine compounds often leads to rapid diffusion from the application site, limiting their effectiveness[11-24].

Immobilization of BAP derivatives in a hydrogel matrix can overcome this limitation by providing controlled release and maintaining a therapeutic concentration for extended periods. Understanding the release kinetics is essential for predicting biological activity, optimizing formulation composition and designing efficient regenerative preparations. The mechanism of release may involve diffusion through water-filled pores, polymer relaxation and interaction between functional groups of the drug and polymer chains.

The aim of this study was to investigate the release kinetics of 6-benzylaminopurine derivatives from a biocompatible hydrogel matrix under physiological conditions and to determine the governing transport mechanisms relevant for regenerative veterinary applications.

Materials and Methods

6-Benzylaminopurine (BAP) derivatives of analytical purity were used as the active substances. Sodium alginate and chitosan were selected as biocompatible polymers for preparation of the hydrogel carrier, and calcium chloride served as the ionic crosslinking agent. Glycerol was applied as a plasticizer to improve flexibility and hydration properties of the material. All solutions were prepared using distilled water and freshly prepared before experiments.

The hydrogel matrix was obtained by dissolving sodium alginate in distilled water under continuous stirring until a homogeneous viscous solution was formed. Chitosan was separately dissolved in dilute acetic acid solution and gradually added to the alginate solution to obtain a uniform polymer mixture. The required amount of BAP derivative was dissolved in a small volume of warm water or ethanol-water mixture and introduced into the polymer composition under constant stirring to ensure even distribution. After complete mixing, glycerol was added to improve elasticity. The resulting composition was slowly introduced into calcium chloride solution, where ionic crosslinking produced a stable three-dimensional hydrogel structure containing immobilized BAP derivative. The formed hydrogel samples were washed with distilled water to remove unbound compounds and stored in sealed sterile containers at 4 °C until use.

Physicochemical properties of the hydrogel were evaluated prior to release experiments. Swelling behavior was determined by immersing pre-weighed hydrogel samples in phosphate buffer solution (pH 7.4) at 37 °C and recording weight changes at specific time intervals. The swelling ratio was calculated from the difference between swollen and initial mass. Structural stability was assessed by observing changes in shape and integrity during incubation.

Controlled release studies were carried out in phosphate buffer solution simulating physiological conditions. Hydrogel samples containing known amounts of BAP derivatives were placed in the release medium at 37 °C under gentle shaking. At predetermined time intervals, aliquots of the solution were withdrawn and replaced with equal volumes of fresh buffer to maintain constant volume and sink conditions. The concentration of released compound was determined spectrophotometrically in the ultraviolet region at the characteristic absorption wavelength of the BAP derivative. A calibration curve constructed from standard solutions was used to calculate cumulative release percentage.

To determine the mechanism of release, experimental data were fitted to common kinetic models including zero-order, first-order, Higuchi and Korsmeyer–Peppas equations. Diffusion exponent values were calculated to identify transport type and contribution of polymer relaxation to drug release.

All measurements were performed in triplicate, and results were expressed as mean values with standard deviation. Statistical analysis was carried out to evaluate reproducibility and reliability of the obtained kinetic parameters.

Results and Discussion

The prepared hydrogel containing 6-benzylaminopurine (BAP) derivatives formed a homogeneous, elastic and mechanically stable structure capable of retaining its integrity in aqueous medium. The material exhibited high hydration ability and quickly absorbed physiological buffer, indicating the presence of an interconnected porous network. After swelling equilibrium was reached, the hydrogel maintained constant mass for a prolonged period, confirming structural stability during the release process (fig-1).

Figure-1. Bu rasmda laboratoriya sharoitida ikki tadqiqotchi ustoz va shogird biofaol material ustida tajriba olib borayotgani tasvirlangan.

Release experiments demonstrated a characteristic biphasic profile. During the initial stage, a moderate release of the BAP derivative occurred, corresponding to diffusion of molecules located near the surface and in larger pores of the polymer matrix. This phase was followed by a slower and prolonged release stage extending over many hours, indicating gradual diffusion from

the inner hydrogel structure. The absence of a sharp burst effect confirmed successful immobilization of the compound within the polymer network(fig-1).

Fig-1. The prepared bioactive hydrogel is being applied to a cow's wound during a veterinary treatment trial.

Kinetic modeling showed that the release process did not follow pure zero-order or first-order behavior. The best correlation was observed with the Higuchi and Korsmeyer–Peppas models. The diffusion exponent values ($0.45 < n < 0.89$) indicated non-Fickian transport, meaning that the release mechanism involved both diffusion of the BAP derivative through water-filled pores and relaxation of polymer chains. This behavior is typical for hydrophilic crosslinked matrices where swelling and polymer rearrangement contribute to mass transfer.

The rate of release depended on swelling degree of the hydrogel. As water penetrated into the matrix, polymer chains expanded and created additional pathways for migration of active molecules. However, interactions between functional groups of the BAP derivative and polymer chains slowed down diffusion, providing sustained delivery. Such interactions likely include hydrogen bonding and electrostatic attraction, which temporarily retain molecules inside the network and regulate their gradual liberation.

Prolonged release is advantageous for regenerative applications because it maintains a stable local concentration of biologically active purine derivatives. Instead of rapid depletion after application, the hydrogel continuously supplies the compound to the surrounding tissue. This can support cell proliferation, fibroblast activity and formation of new tissue structures for an extended period. The absence of rapid release also reduces the need for frequent reapplication and improves treatment efficiency under veterinary conditions.

Overall, the obtained results confirm that the developed hydrogel matrix functions as an effective controlled-release carrier for 6-benzylaminopurine derivatives. The combined influence of diffusion and polymer relaxation ensures sustained delivery, which is particularly suitable for regenerative therapeutic systems requiring long-term biological stimulation.

Conclusion

The study confirmed that incorporation of 6-benzylaminopurine derivatives into a biocompatible hydrogel matrix provides an effective controlled-release system suitable for regenerative veterinary applications. The developed material demonstrated stable structure, high water-retention capacity and the ability to maintain prolonged release of the biologically active compound under physiological conditions.

The sustained liberation of BAP derivatives ensured continuous local stimulation of reparative processes, supporting cell proliferation and tissue restoration while minimizing rapid depletion of the active substance. Such release behavior reduces the need for frequent application and improves treatment efficiency in practical livestock management.

Overall, the hydrogel carrier functions not only as a protective wound covering but also as a regulator of therapeutic delivery. The obtained results indicate that the proposed system is a promising platform for development of long-acting veterinary regenerative preparations and can be further optimized for clinical use in treatment of animal skin injuries and inflammatory lesions.

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