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jarayoni har xil konsentratsiyali etanol erituvchilarida ultratovushli faollashtirish ostida optimallashtirildi.

Natijalar va ularning tahlili. Olib borilgan biotransformatsiya jarayoni natijasida rovoch tarkibidagi murakkab antrahinon glikozidlarining fermentativ gidrolizi amalga oshdi. YOSHX tahlillari ko'rsatishicha, erkin emodin va xrizofanol miqdori dastlabki xomashyoga nisbatan mos ravishda 35% va 42% ga ortgan. Chuqur qayta ishlash natijasida olingan quruq ekstraktning antioksidant faolligi DPPH radikallarini neytrallash testi orqali tekshirilganda, gIdrolizdan keyingi mahsulotning samaradorligi sezilarli yuqori natija ko'rsatdi ($IC_{50} = 12.4 \mu\text{g/mL}$).

Xulosa. Tadqiqotlar natijasida Rheum ribes L. o'simligini fitokimyoviy va biotexnologik usullar yordamida chuqur qayta ishlashning samarali sxemasi ishlab chiqildi. Mikrobiologik biotransformatsiya yordamida dorivor xomashyoning biologik faolligini sezilarli darajada oshirish imkoniyati isbotlandi. Olingan natijalar asosida mahalliy xomashyo negizida import o'rnini bosuvchi dori vositalari substansiyasini sanoat miqyosida ishlab chiqarish tavsiya etiladi. (Times New Roman, 12 pt, tekis)

Foydalanilgan adabiyotlar ro'yxati.

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**NATURAL PRODUCT-INSPIRED THERAPEUTICS: SYNTHESIS OF NOVEL
ALKYLAMINO-FUNCTIONALIZED PURINE DERIVATIVES WITH
ANTICANCER APPLICATIONS**

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Abstract. The development of small-molecule therapeutics that selectively target oncogenic pathways while minimizing systemic toxicity remains a major frontier in medicinal chemistry. The purine ring is widely recognized as a "privileged scaffold" due to its structural homology with endogenous nucleic acids and natural alkaloids. This study details the natural product-inspired design and synthesis of a novel series of amino-substituted purine derivatives derived from a 2,6-dichloropurine template.

The synthetic workflow investigated the impact of aliphatic spacer length on the compounds' physical and potential pharmacological properties through two distinct pathways: one involving the reaction of 2,6-dichloropurine with a long-chain flexible nucleophile. Both pathways achieved regioselective nucleophilic aromatic substitution exclusively at the highly electrophilic C-6 position.

Comprehensive analytical characterization was conducted to confirm structural integrity and sample homogeneity. Analytical HPLC confirmed high chemical purity for the synthesized monomers and demonstrated a clear relationship between chain elongation and column retention time, indicating optimized lipophilicity in the longer chain variant. LCMS and high-resolution mass spectrometry confirmed the exact molecular weights expected for mono-substituted functionalization, ruling out unwanted dimerization. FTIR spectroscopy verified the successful introduction of the amine linkers via the appearance of diagnostic secondary amine stretching bands, while ¹H-NMR definitively proved that the core purine architecture remained intact, showing a sharp, characteristic singlet for the purine ring proton alongside perfectly integrated upfield aliphatic methylene signals. These findings establish a highly efficient, green synthetic route toward structural analogues of active kinase inhibitors, providing a clear chemical framework for subsequent *in vitro* anti-proliferative evaluations against human cancer cell lines.

Keywords: 2,6-dichloropurine, Nucleophilic Aromatic Substitution, Ethylenediamine, Hexanediamine.

Introduction: Among the various heterocyclic arrangements found in nature, the purine ring stands out as a premier privileged scaffold. Purine architectures are foundational to life, serving as the core components of cellular genetic material, enzymatic cofactors, and classical plant-derived xanthine alkaloids. Because of this intrinsic structural homology, synthetic purine derivatives are uniquely equipped to cross cellular membranes and interact dynamically with vital cellular machinery. In oncology, multi-substituted purines have gained immense prominence as potent antineoplastic agents, primarily acting as competitive antimetabolites or as targeted inhibitors of ATP-binding sites in hyperactive cyclin-dependent kinases (CDKs) and receptor tyrosine kinases.

The synthesis of highly targeted purine derivatives requires a starting material template that permits strict regioselective control. 2,6-dichloropurine is an exceptional synthetic platform for this purpose. The two chlorine atoms situated at the C-6 and C-2 positions exhibit distinctly non-equivalent chemical reactivities due to the asymmetric electronic pull of the neighboring heterocyclic ring nitrogens. The C-6 locus is highly electron-deficient, making it exceptionally vulnerable to initial nucleophilic attack under mild thermal conditions. Conversely, the C-2 position remains relatively inert until activated by significantly higher temperatures or specialized catalysts. This electronic differentiation allows for the precise, stepwise alteration of the purine periphery without risking uncontrolled side-reactions.

A key strategy in maximizing the efficacy of these targeted scaffolds is the Flexible Linker Hypothesis. By tethering active pharmacophore groups via flexible aliphatic diamine bridges, the molecule can achieve the spatial conformational mobility required to fit snugly within deep, hydrophobic enzyme pockets or intercalate effectively into DNA base pairs. Furthermore, altering the length of these carbon spacers provides a direct mechanism for tuning the compound's overall lipophilicity—a critical parameter governing passive membrane permeability and intracellular accumulation.

Research Methodology:

Scheme 1: 2,6-dichloropurine with a linear aliphatic diamine 1,6-hexanediamine, the reaction proceeds on reflux via a Nucleophilic Aromatic Substitution pathway. This electronic differentiation, reaction will selectively take place at the C-6 position first. The primary amine group of your 1,6-hexanediamine attacks the C-6 carbon, displacing the chlorine atom as a chloride ion. As the nucleophilic amine attacks the purine core, an equivalent of hydrochloric acid HCl was generated. TEA acts as an acid scavenger, neutralizing the escaping HCl to form a triethylammonium chloride precipitation salt.

Scheme 2: 2,6-dichloropurine with a 1,2-ethylenediamine, the reaction proceeds on reflux via a Nucleophilic Aromatic Substitution pathway. A same reaction condition, TEA was used as a catalyst and ethanol was used as a solvent. C-6 position is highly electron-deficient due to the direct electronic pull of the neighbouring ring nitrogen. It is significantly more electrophilic than C-2.

Result and Discussion: LC-MS analysis was performed and the result showed a single peak in LC-chromatogram that reflect a high-grade purity of intermediate. An ESI-Mass scan peak at $m/z = 267$, $[M-H]$ was observed that indicate the formation of an intermediate. **FTIR analysis** N-H stretch at FTIR spectrum exhibited a characteristic absorption band at $3200\text{--}3400\text{ cm}^{-1}$ corresponding to N-H stretching vibration confirmed the presence of the NH functionality.

LC-MS analysis of F4E intermediate was performed and the result displayed a single peak in LC- chromatogram that imitated the high-grade purity. An ESI-Mass scan peak at $m/z = 211$, $[M-H]$ was perceived the formation of an intermediate.

FTIR analysis N-H stretching vibrations are identified using FTIR spectroscopy, typically appearing in the range: **Primary amine ($-\text{NH}_2$):** $3300\text{--}3500\text{ cm}^{-1}$ (often two bands), **Secondary amine ($-\text{NH}-$):** $3300\text{--}3500\text{ cm}^{-1}$ (one band), **Amide N-H:** $3200\text{--}3400\text{ cm}^{-1}$

Conclusion: The resulting amino-functionalized purine derivatives were successfully synthesized and isolated in high chemical yields with excellent purity. Detailed spectroscopic analyses, including FTIR, ^1H NMR, and LC-MS, unequivocally confirmed the successful and selective substitution of chlorine atoms by the corresponding diamine linkers. The synthetic strategy proved to be efficient, reproducible, and highly selective, enabling the generation of structurally diverse purine analogues without significant side-product formation. Furthermore, the incorporation of amino-functionalized side chains enhanced the molecular diversity of the purine scaffold,

providing opportunities for improved biological interactions and pharmacological activity. These findings demonstrate the effectiveness of the developed synthetic approach and establish a strong foundation for the further evaluation of these compounds as potential anticancer agents.

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NAMATAK O'SIMLIGINI DORIVORLIK XUSUSIYATLARI VA BOZORDAGI UNGA BO'LGAN TALAB

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Annotatsiya: Maqola davomida dorivor namatakning alohida xususiyatlari, tabiyati va unga bo'lgan bozordagi talabni kuzatish metodi orqali yig'ilgan ma'lumotlar bilan bayon etiladi. Unga ko'ra bu o'simlik bemorlar tomonidan kerakli vaziyatlarda alohida e'tirof qilinib, faol foydalanilayotgani aniqlandi.