

# Ketoconazole: A Review of its Antifungal Properties and Clinical Applications

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**Abstract:** Ketoconazole (KET), an imidazole derivative with well-known antifungal properties, is lipophilic and practically insoluble in water, therefore its clinical use has some practical disadvantages. The aim of the present study was to investigate the influence of PAMAM-NH<sub>2</sub> and PAMAM-OH dendrimers generation 2 and generation 3 on the solubility and antifungal activity of KET and to design and evaluate KET hydrogel with PAMAM dendrimers. It was shown that the surface charge of PAMAM dendrimers strongly affects their influence on the improvement of solubility and antifungal activity of KET. The MIC and MFC values obtained by broth dilution method indicate that PAMAM-NH<sub>2</sub> dendrimers significantly (up to 16-fold) increased the antifungal activity of KET against *Candida* strains (e.g., in culture *Candida albicans* 1103059/11 MIC value was 0.008 µg/mL and 0.064 µg/mL, and MFC was 2 µg/mL and 32 µg/mL for KET in 10 mg/mL solution of PAMAM-NH<sub>2</sub> G2 and pure KET, respectively). Antifungal activity of designed KET hydrogel with PAMAM-NH<sub>2</sub> dendrimers measured by the plate diffusion method was definitely higher than pure KET hydrogel and than commercial available product. It was shown that the improvement of solubility and in the consequence the higher KET release from hydrogels seems to be a very significant factor affecting antifungal activity of KET in hydrogels containing PAMAM dendrimers.

**Keywords:** PAMAM dendrimer; ketoconazole; hydrogel; antifungal activity; aqueous solubility

## REFERENCES

- [1]. Ketoconazole: A Review of its Therapeutic Efficacy in Superficial and Systemic Fungal Infections, Drug Evaluations, Published: 18 November 2012, Volume 23, pages 1–36, (1982).
- [2]. Topical ketoconazole: a systematic review of current dermatological applications and future developments Franchesca D. Choi, Margit L.W. Juhasz & Natasha Atanaskova Mesinkovska ORCID Icon, Pages 760-771
- [3]. <https://www.ncbi.nlm.nih.gov/books/NBK559221/>
- [4]. <https://www.sciencedirect.com/topics/chemistry/ketoconazole#:~:text=Ketoconazole%20has%20a%20broad%20spectrum,respect%20to%20staphylococci%20and%20streptococci.>
- [5]. <https://en.m.wikipedia.org/wiki/Ketoconazole>
- [6]. Ketoconazole: a review of its therapeutic efficacy in superficial and systemic fungal infections
- [7]. R C Heel et al. Drugs. 1982 Jan-Feb. Hide details Drugs. 1982 Jan-Feb; 23(1-2): 1-36.
- [8]. Doi: 10.2165/00003495-198223010-00001. R C Heel, R N Brogden, A Carmine, P A Morley, T M Speight, G S Avery.
- [9]. <https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/ketoconazole>
- [10]. BRIEF RESEARCH REPORT article, Front. Drug Discov., 29 August 2022
- [11]. Sec. Anti-Infective Agent, Volume 2 – 2022 | <https://doi.org/10.3389/fddsv.2022.1000827>
- [12]. Antifungal properties of (2S, 4R)-Ketoconazole sulfonamide analogs
- [13]. <https://www.mayoclinic.org/drugs-supplements/ketoconazole-topical-route/side-effects/drg-20067739?from=results&fromopen=1>
- [14]. Hydrogel of Ketoconazole and PAMAM Dendrimers: Formulation and Antifungal Activity
- [15]. By Katarzyna Winnicka 1,\*ORCID, Magdalena Wroblewska 1, Piotr Wiczorek 2, Pawel Tomasz Sacha 2 and Elzbieta Tryniszewska, Molecules 2012, 17(4), 4612-4624.
- [16]. [https://my.clevelandclinic.org/health/drugs/18899-ketoconazole-cream.](https://my.clevelandclinic.org/health/drugs/18899-ketoconazole-cream)

- [17]. Natural Oils Enhance the Topical Delivery of Ketoconazole by Nanoemulgel for Fungal Infections Irfan Ahmad, Ms Farheen, Ashish Kukreti, Obaid Afzal\*, Md Habban Akhter, Havagiray Chitme, Sharad Visht, Abdulmalik Saleh Alfawaz Altamimi, Manal A. Alossaimi, Ebtisam R. Alsulami, Mariusz Jaremko, and Abdul-Hamid Emwas
- [18]. Cite this: ACS Omega 2023, 8, 31, 28233–28248.
- [19]. Ketoconazole: A review of a workhorse antifungal molecule with a focus on new foam and gel formulations, June 2008 Drugs of today (Barcelona, Spain: 1998) 44(5):369-80.
- [20]. <https://pubs.rsc.org/en/content/articlehtml/2023/md/d3md00151b>.