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## ENVIRONMENTAL CONDITIONS IN THE SYNTHESIS OF MONASTROL

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The synthesis of eutectic mixtures based on 3- (carboxymethyl) -1-vinyl-1H-imidazole-3-ium (chloride, bromide, hexofluorophosphate) and thiourea in various ratios (from 2: 1 to 1: 3) was realized, the aggregate state and established catalytic activity for the synthesis of Monastrol, which showed a wide range of pharmacological activity.

The most effective method currently used for the synthesis of dihydropyrimidines remains the well-studied multicomponent Biginelli reaction [1]. The Biginelli reaction, which is commonly used for the direct preparation of Monastrol and its derivatives, has many advantages over traditional synthetic methods [2]. Three-component and one-pot synthesis under Biginelli reaction conditions makes it possible to obtain monastrol based on the result of the interaction of acetoacetic ester, thiourea, and 3-hydroxybenzaldehyde in the presence of various eutectic catalysts and various solvents and without them [3]. From the point of view of environmentally friendly conditions, they have the advantage of many reagents collected in one vessel, which avoids waste from multi-stage purification and the formation of residues.

The biological role of Monastrol has led to significant interest in its synthesis and is a 3-component one-pot synthesis based on the interaction of acetoacetic ester, thiourea and 3-hydroxybenzaldehyde, which avoids waste from multi-stage purification and the formation of residues. The synthesis is catalyzed by inorganic acids, ionic liquids, eutectic solvents, or under microwave irradiation. As a result of compounds as catalysts, a yellowish-gray crystalline substance was obtained as a result, the physicochemical constants of which, including  $Tm = 182-184^{0}C$ , indicated the formation of monastrol, the yield of which was 40%. The maximum yield of the product was 79%.

In the synthesis of Monastrol, the goal is to select reagents and test various catalysts that are environmentally friendly, least toxic and financially attractive in order to maximize product yield, reduce reaction time, selectivity and minimize reagent surpluses, formation of by-products, high temperatures, environmental pollution. environment, waste and costs. Catalysis plays a fundamental role in Biginelli synthesis, especially in developing strategies to approach eco-friendly catalytic conditions for further use in the renewable chemical industry [4].

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## References

- 1. Vdovina, S.; Mamedov, A. New possibilities of Biginelli reaction. In: Advances in chemistry, 2008, 77(12), pp. 1091-1128.
- 2. Oliver, Kappe, C.; Shishkin, O.; Uraya, G.; Verdinoa, P. X-Ray Structure, Conformational Analysis, Enantioseparation and Determination of Absolute Configuration of the Mitotic Kinesin Eg5 Inhibitor Monastrol. In: BMC Chem Biol, (6:2), 2006.
- 3. De Bonis, S. et al. Interaction of the mitotic inhibitor monastrol with human kinesin Eg5. In: Biochemistry, 2003, (42), pp. 338-349.
- 4. Macaev, F. Green chemistry protocols: specific ionic liquids as recyclable reagents, catalysts, solvents and extractors. Environmental Security Assessment and Management of Obsolete Pesticides in Southeast Europe. In: SPRINGER Science&Business media, 2013. pp. 313-331.