INTRODUCTION:
The steroid scaffold is present in many FDA-approved drugs for the treatment of various diseases such as inflammation, allergic reaction, heart disease, cancer, and metabolic disease. The steroid skeleton is a favorable scaffold for the design and development of novel agents with pharmacological activity because even a small change in the molecular structure of such molecules. This approach proved as an excellent strategy for obtaining potent cytotoxic agents. O-Alkyl derivatives of oximes containing the H-bond-accepting group can change activity against cancer cells.

OBJECTIVES:
The aim of this work was the synthesis of new steroid O-substituted (16E)-oximes with and without H-bond-donating group as well as in silico assessment of their physicochemical properties and pharmacokinetics.

METHOD / DESIGN:
The structures of synthesized compounds were determined based on their spectral data. In silico ADMET properties were studied for all synthesized compounds using SwissADME and ProTox-II web tools.

The Bioavailability Radar, which takes into account six physicochemical properties: lipophilicity, size, polarity, solubility, flexibility, and saturation, showed that all parameters of the synthesized compounds were in the optimal range.

The drug-likeness evaluation revealed that synthesized compounds fulfill the requirements of the five different rule-based filters (Lipinski, Weber, Egan, Ghose, and Muegge).

Lipinski: MW ≤ 500; HBD ≤ 5; HBA ≤ 10; LogP ≤ 5
Weber: LogP ≤ 5.8; TPSA ≤ 131.6 Å²
Egan: LogP ≤ 5.8; TPSA ≤ 131.6 Å²
Ghose: MW ≤ 160 ≤ 480; 0.4 ≤ LogP ≤ 5.6; 40 ≤ MR ≤ 130; 20 ≤ atom ≤ 70
Muegge: MW ≤ 200; ≤ 600; ≤ 2 ≤ LogP ≤ 5; TPSA ≤ 150 Å²; num.rings ≤ 7; num. carbons ≤ 4; num. heteroatoms ≤ 1; rotatable ≤ 15; HBD ≤ 5; HBA ≤ 10

Prediction of pharmacokinetic behavior showed that tested compounds could be absorbed by the human intestine but couldn't cross the blood-brain barrier (except 2).

Restrained synthetic 16E-oximes were prepared from dehydroepiandrosterone (16E)-oxime.

New steroidal O-substituted (16E)-oximes were prepared from dehydroepiandrosterone (16E)-oxime.

Androstan derivatives 2, 3, and 5 did not show inhibition effect on five major isoenzymes (CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4) involved in the metabolic drug elimination.

Compounds 3-7 were found to bear a low risk of being mutagenic and carcinogenic, while carcinogenicity was predicted for compound 2.

CONCLUSIONS:
In silico ADMET analysis showed that synthesized derivatives of dehydroepiandrosterone (16E)-oxime possess drug-like properties, and compounds 2-6 have better safety profile than 1.