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# DEVELOPMENT AND VALIDATION OF GAS CHROMATOGRAPHY METHODS FOR THE CONTROL OF VOLATILE IMPURITIES IN THE PHARMACEUTICAL SUBSTANCE DUTASTERIDE

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Dutasteride, N-[2,5-Bis(trifluoromethyl)phenyl]-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide, is an active pharmaceutical ingredient (API) which inhibits the conversion of testosterone to dihydrotestosterone. Dutasteride as a 5-reductase inhibitor is useful for the treatment of benign prostatic hyperplasia (BPH) and prostate cancer.

Because of a large variety of solvents and reagents used in the synthesis, it was necessary to develop new, sensitive and selective gas chromatography (GC) methods. The optimization of the methods consisted in selecting different types of sample injection and detection as well as optimization of experimental conditions that allowed to meet the appropriate range (10-120% of the specification limit) and suitable detection limits (LOD) of compounds. Significant differences in the volatility of these compounds forced the division into volatile solvents (methanol, acetonitrile, dichloromethane, ethyl acetate, heptane and toluene) analyzed with the use of the gas chromatography with headspace (GC-HS) and less volatile compounds (pyridine, dimethylformamide, 1,4-dioxane, acetic acid, ethylene glycol, 4-dimethylaminopyridine) analyzed with the use of gas chromatography with direct injection (GC-FID). Benzene, carbon tetrachloride and 1,2-dichloroethane are potential contaminants of toluene and dichloromethane, thus the control of these solvents was a limit test procedure. Due to the low specification limits for benzene (2 ppm), carbon tetrachloride (4 ppm) and 1,2-dichloroethane (5 ppm) it was neccesery to use gas chromatography with mass spectrometry detection (GC-MS).

All three new methods were validated according to the requirements of the ICH (International Conference on Harmonization) validation guideline Q2R1 and the guideline for residual solvents Q3C. Specificity, precision, accuracy, linearity, limits of detection and quantitation and robustness were determined and the results meeting the acceptance criteria were obtained.

**The form of the presentation proposed by the Author (delete if inappropriate):**
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