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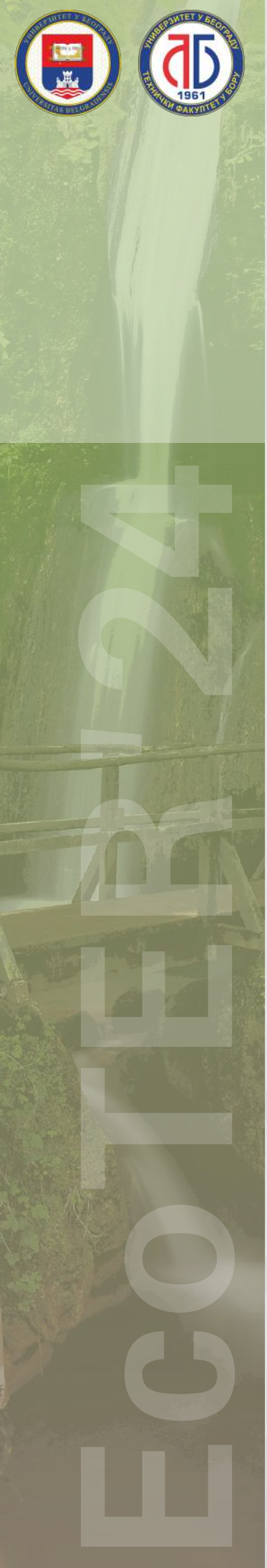

31st International conference

Ecological Truth & Environmental Research

Editor
Prof. Dr Snežana Šerbula

PROCEEDINGS

Hotel Sunce, Sokobanja, Serbia
18–21 June 2024

PROCEEDINGS

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SUSTAINABLE SOLUTIONS IN ANALYTICAL CHEMISTRY: COMBINING OF INSTRUMENTAL TECHNIQUES AND ENVIRONMENTAL-FRIENDLY NATURAL INDICATORS FOR CLASSICAL VOLUMETRY

ODRŽIVA REŠENJA U ANALITIČKOJ HEMIJI: KOMBINACIJA INSTRUMENTALNIH TEHNIKA I EKOLOŠKI PRIHVATLJIVIH PRIRODNIH INDIKATORA ZA KLASIČNU VOLUMETRIJU

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Abstract

Dimethyl fumarate (DMF) serves as the active ingredient in medications designed to treat relapsing forms of multiple sclerosis, yet there is a notable absence of specific monographs for this compound in available pharmacopeia's. Nevertheless, various instrumental chromatographic techniques are employed to determine the concentration of DMF across diverse matrices.

This study endeavours to highlight the viability of merging structural instrumental analytical methods with a simple classical volumetric approach utilizing a cost-effective, non-toxic, and natural indicator - the ethanol extract of *Curcuma longa* powder. The primary aim is to accurately determine DMF assay in commercial samples without utilizing certified reference materials (CRM).

Samples of DMF procured from a commercial supplier underwent analysis employing instrumental techniques including GC/MS, IR, and NMR. An innovative titrimetric method for determining DMF content involved ultrasonically assisted alkaline hydrolysis by sodium hydroxide solution at 70°C for 15 minutes, followed by back titration of excess alkali using a standard hydrochloric acid solution and the ethanol extract of *Curcuma longa* powder as an indicator. To evaluate the analytical validity of this innovative method, a modified standard method for ester content determination served as a comparative benchmark. This standard method entails alkaline hydrolysis of the DMF sample by sodium hydroxide solution, boiling for 30 min, and subsequent back titration of excess alkali with a standard hydrochloric acid solution, employing phenolphthalein as indicator.

GC/MS analysis revealed a significant DMF content in the sample (99.9%), with the detection of a 0.1% cyclic dimer of dimethyl fumarate, specifically the tetramethyl ester of

1,2,3,4-cyclobutanetetracarboxylic acid (TMCBA). However, these findings necessitate careful interpretation as they exclusively relate to the compound's gaseous phase. The IR spectrum exhibited characteristic absorption bands for DMF, alongside a broad absorption band at 3400 to 3000 cm^{-1} region, indicative of fumaric acid (FA). Proton NMR analysis highlighted dominant peaks for DMF protons (6.7 and 3.7 ppm) and low-intensity peaks around 6.6 ppm, potentially arising from protons attached to α-C atoms of FA carboxyl groups. Regarding volumetric techniques for DMF assay determination, it is important to emphasize that during the alkaline hydrolysis procedures, all detected fumarate compounds present in the commercial material (DMF, TMCBA, and FA) were successfully converted to sodium fumarate, with their total content expressed as DMF. Finally, the result of the DMF assay obtained using the innovative volumetric method (99.4%, n=5) did not show a statistically significant difference compared to the DMF content determined using the standard volumetric method (99.3%, n=5).

Instrumental analyses suggest that the investigated DMF sample exhibits high purity (>95%) with low-level impurities (TMCBA and FA), a conclusion supported by DMF content results obtained through both standard and innovative volumetric methods (>99%). Ultimately, the combining of described instrumental techniques with the innovative method for DMF assay determination, using environmental friendly ethanol extract of *Curcuma longa* powder as indicator, represents a successful analytical tool for quantifying DMF content without CRM.

Keywords: dimethyl fumarate analysis, instrumental techniques, environmental-friendly indicator, Curcuma longa, volumetric analysis.

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