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Green Chemistry Spectrofluorimetric Assessment of Folic Acid in Pharmaceutical Formulations Using Acriflavine as an Efficient Fluorescent Probe

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Abstract

A sensitive, simple, inexpensive, rapid, and eco-friendly spectrofluorimetric method was created to assess the folic acid (FA) concentration in tablets using acriflavine (ACF) as an eco-friendly photoprobe. Based on its ability to quench the ACF fluorescence intensity in water at pH 8.0 and $\lambda_{ex} = 460$nm. FA concentration was measured by quenching the fluorescence intensity of the ACF at $\lambda_{em} = 508$ nm within the linear range of 3.5×10^{-6}–30.0×10^{-6} mol L^{-1} with a correlation coefficient $r^2 = 0.9991$. The limit of quantification (LOQ) and the limit of detection (LOD) are 1.159×10^{-6} mol·L^{-1} and 0.383×10^{-6} mol·L^{-1}, respectively. This method was easy to use and accurately and effectively evaluated FA in pharmaceutical tablet samples. No influence was observed from the excipients usually contained in pharmaceutical formulations. The method was verified as valid according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines. In addition, its greenness has been estimated using environmental assessment tools.

Keywords

Acriflavine, folic acid, fluorescent assay, greenness evaluation, eco-friendly

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Introduction

Folic acid (FA) or folate (Figure 1a) is a vital nutritional agent for humans and other mammals, playing a role in several events that contribute to DNA synthesis.[1] It is a water-soluble vitamin that cannot be generated or stored in the human body, resulting in its continuous loss, which suggests problems with FA deficiency. It is classified as an anti-anemia and growth agent that can stimulate the production of RBCs. In addition, FA supplementation during pregnancy can lower the risk of newborn congenital heart defects and prevent neural tube defects.[2,3] FA deficiency is linked to several neurological issues, such as depression, stroke, and Alzheimer's disease. Additional symptoms include poor growth, heart palpitations, fatigue, swollen tongue, and hearing loss.[3,4] The European Union has authorized a daily intake of 400 µg for adults. FA can be obtained from medications and dietary supplementation to reduce this risk. Different methods are used for assessing FA, such as electrochemical detection,[5] capillary zone electrophoresis,[6] chemiluminescence,[7] and various liquid chromatographic techniques, e.g., liquid chromatography–mass spectrometry (LC-MS),[8,9] high-performance liquid chromatography (HPLC),[10,11] ultra-HPLC,[12] and fluorescence detection.[13,14]

Most of these methods have some disadvantages. The spectrophotometric methods have a narrow range of determination, extraction, or heating; the reaction takes a long time, and the colored product formed is unstable.[15] Chromatographic methods are expensive and require intricate purification processes and extraction.[16] Also, the electroanalytical technique is poorly sensitive.[8]

Recently, fluorescent sensors have been in greater demand due to their high sensitivity, selectivity, speed, real-time processing capabilities, and ability to identify targets visually. The accessibility of spectrofluorimetric techniques may benefit quality control evaluations and laboratories that lack access to costly or complex methods. Moreover, with no multiple

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