Stability of 2,5 mg folic acid capsules

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Introduction

In neonatal reanimation and neonatology, folic acid (FA) is used to correct macrocytosis anaemias during premature infants first weeks of life when iron injections are not effective to cure them. Then, the usual posology is 2,5 mg/d, but marketed tablets are dispensed in 5 mg forms, .

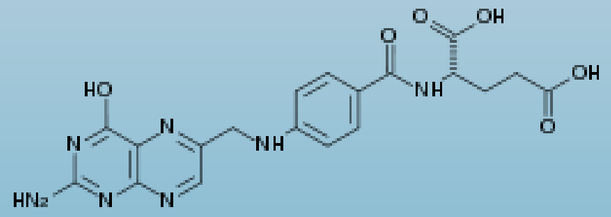
→ **Purpose** : Elaboration of 2,5mg folic acid hospital preparation, development of its assay method and study of its stability.

Equipment and method

1. Formulation
   - Folic acid : 2,5 mg
   - QS monohydrate lactose to produce 100 capsules n°44
2. HPLC – Instrumentations and analytical requirements
   - HPLC : Hitachi® L-2130, DAD L2455, EZChrom Elite® software.
   - Column : Kinetex® 5 µ, C18, 100A, 150x4,6 mm
   - Mobile phase : Water/Methanol *R* (88/12), phosphate buffer, flow : 0,6 mL/min, injection volume : 20 µL.
3. Forced degradation study (GERPAC stability guide)

Folic acid is subjected to various degradation conditions : acid and basic hydrolysis (HCl and NaOH respectively), thermal, photodegradation and oxidation (H_2O_2).

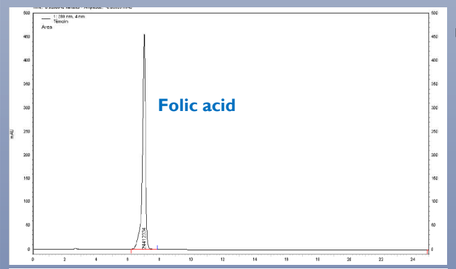
4. Assay method validation procedure (ICH/SFSTP) : linearity in concentration range [35 - 65] µg/L for target concentration of 50 µg/L, matrix effect, reproducibility, repeatability, accuracy.
5. Stability : over a year, in 21 ± 2°C and 50 ± 5 % residual humidity, opaque blister packing.



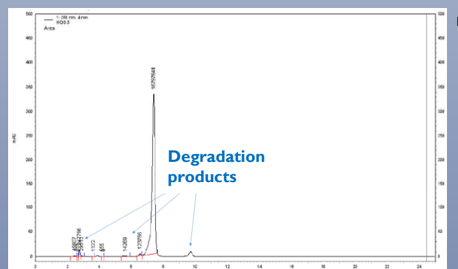
Folic acid

Results

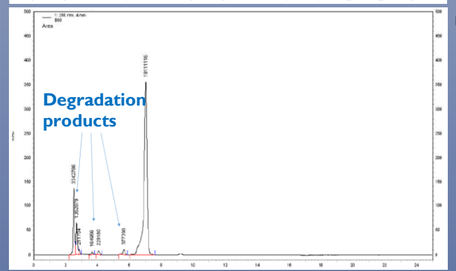
I. Forced degradation study



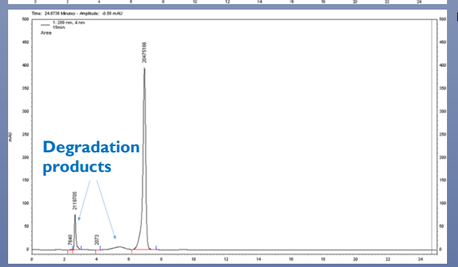
- Control



- Oxidation : 20 % of folic acid is degraded in 3 % H202 when heated to 80° C.



- Photodegradation : 15 min exposition to natural light, about 15 % of degradation.



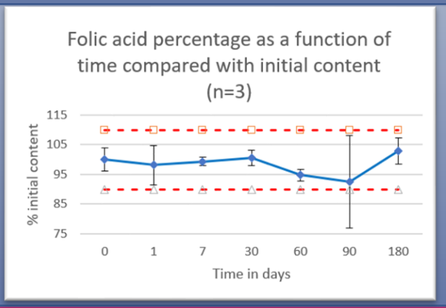
- Hydrolysis : no effect in basic condition, but in acid (0,5 M HCl) : ≈ 25 % degradation of folic acid.

II. Validation method

Method is linear in concentration range [35 - 65] µg/L (p_{value} > 0,05 alpha risk 5 %).
No significant matrix effect was found with a 5 % alpha risk.
Method is repeatable (CV = 1,84 %), reproducible (CV = 2,12 %) and accurate [98,85 - 101,23] % for target concentration of 50 µg/L.

III. Stability

Batch content uniformity was controlled on 10 capsules (PE 2.9.6).
Peak's purity were always verified in each chromatogram.
No degradation product was viewed.
Powder appearance was unchanged.



→ **Conclusion** : Folic acid capsules remain stable for, at least, 6 months in an appropriate form for routine use and to anticipate needs of both units.