

# Quality assessment of 3D printed sildenafil and furosemide tablets for the pediatric population using an innovative extrusion-based technique

## Background and importance



Commercially available tablets often don't meet patient's need, as is the case for **children**.

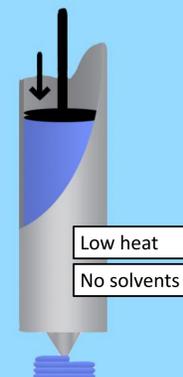


A 3D printer can produce **personalised medicine**, but a suitable technique is needed for chemically unstable drugs

## Materials and methods

Cartridges containing formulations with **furosemide** 2 mg or 10 mg per tablet, or **sildenafil** 4 mg per tablet, were slightly heated to a semi-solid consistency to allow printing.

3D printed tablets were analysed on quality requirements of the European Pharmacopoeia (EP) in triplicate. Linear regression analysis was performed to assess correlation between tablet mass and content.



### Did you know?



Furosemide and sildenafil are available in oral liquid form. However, the liquid with furosemide contains propylene glycol to ensure a solution, and the solution of sildenafil has a poor taste. A suspension of sildenafil with better taste acceptability is also available, but suspensions have the intrinsic risk of dosage errors.



EP 2.9.5  
Weight distribution



EP 2.9.40  
Content uniformity



EP 2.9.3  
Dissolution profile

## Aim and objectives

A **proof-of-concept** study was conducted using a low heat, solvent-free extrusion-based 3D printing technique.

The **quality requirements** as stated by the European Pharmacopoeia (EP) were evaluated.

### Quality control



## Results

Test	EP Requirement	Furosemide 2 mg	Furosemide 10 mg	Sildenafil 4 mg
 Content uniformity	Acceptance value of 15	4.2 – 10.6	4.8 – 8.9	6.6 – 9.2
 Dissolution profile	>80% dissolved content after 45 min	76.9% (95%-CI 73.6 – 80.2%) Complied with S <sub>2</sub> -level	86.3 – 88.8%	86.6 – 89.7%



The tablets met the weight distribution requirements only after adjusting the printing path to **double row printing**. The average weight was 141.1 mg with an RSD of 1.26%

In addition to performed tests, the EP also describes quality tests to ensure **microbiological stability** (EP 5.4.1) and **mechanical strength** (EP 2.9.7 and EP 2.9.8)



All tablets showed **linear correlation** between tablet mass and tablet content.

### Discussionpoint 1. Testing of mechanical strength



The EP describes friability (EP 2.9.7) and resistance to crushing (EP 2.9.8) to assess the mechanical strength of tablets. However, for 3D printed tablets, these tests may be too rigorous. A test designed to ensure layer adhesion may be more appropriate.

### Discussionpoint 2. Appropriateness of tests for small batches



For small batch sizes it may not be practical to carry out all quality tests. In such cases, the EP allows for other suitable methods to ensure quality. It therefore can be argued that for 3D printed tablets, other methods should be investigated to assess suitability.

## Conclusions



**Successful** proof-of-concept study of an innovative 3D printing technique

Further investigation of suitable quality tests for 3D printed tablets will be performed in further studies.



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