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FORMULATION OF TACROLIMUS SOLUTION FOR SUBLINGUAL USE

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Background

Tacrolimus is an immunosuppressive agent used in solid organ transplantation (SOT) for prophylaxis of rejection. In our hospital SOT are performed including rare multivisceral transplantations (MTVx). There are clinical situations when oral tacrolimus can't be administered to the MTVx patient, because of non-functional bowel. In home care, patient could be treated with tacrolimus for sublingual use. There is no commercial product for sublingual administration available, so formulation has to be developed.

Tacrolimus is practically insoluble in water, however, suspension can be prepared using tacrolimus capsule powder content. This formulation is unstable with risk of sedimentation, therefore uniform dose can't be achieved. We used solubility of tacrolimus in ethanol and prepared the homogenous sublingual solution from substance.

Material and methods

Tacrolimus solution for sublingual use 10 mL	
Concentration	**10 mg/mL**
Ingredient listing	**Qty. [g]**
Tacrolimus monoh.	**0.10**
Ethanol 96%	**3.00**
Glycerol 85%	**8.00**
Sweet orange oil	**0.06**
Polysorbate 80	**0.05**
Citric acid 5%	**q.s.**

Tacrolimus was dissolved in ethanol 96%
↓
Glycerol 85% was slowly added
↓
Sweet orange oil and Polysorbate 80 were added for higher palability
↓
Citric acid 5% was used to adjust pH

Aim and objectives

- To formulate solution of tacrolimus 10 mg/mL based on ethanol and glycerol.
- To describe the preparation, container, storage conditions and shelf-life of tacrolimus solution for sublingual use.

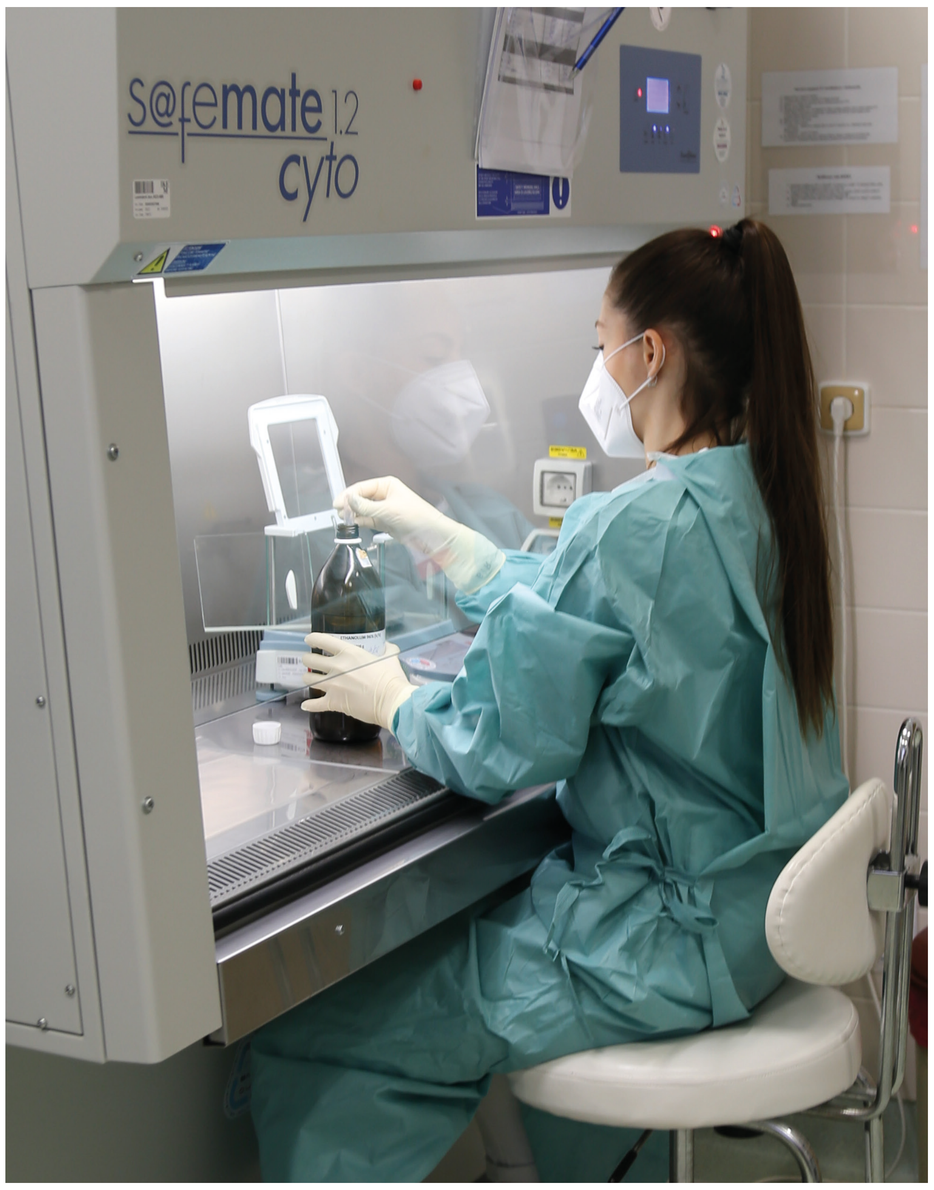

Fig. 1

Ingredient-specific information	Tacrolimus
Hazardous substance H 361 (reprotoxics)	
Bilological safe cabinet (BSC) is recommended	

Results

Tacrolimus solution for sublingual use	
Concentration	**10 mg/mL**
Organoleptic properties	**Turbid and homogenous suspension with orange scent**
pH	**4 to 6**
Storage	**15-25 °C**
Shelf-life	**30 days**

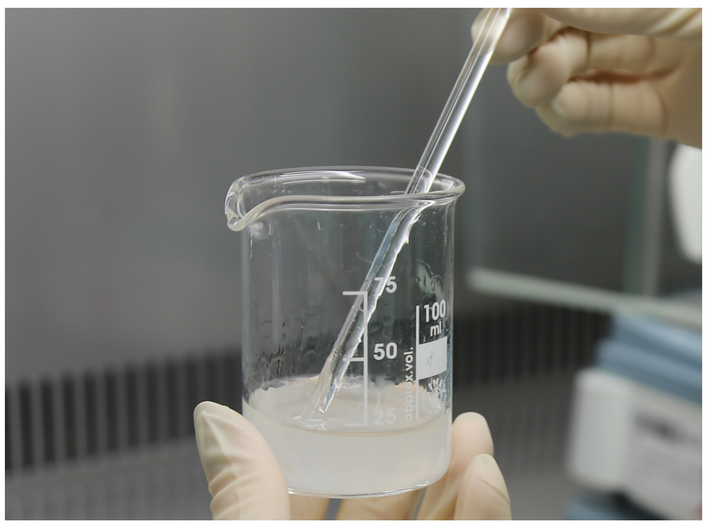

Fig. 2
Solution was prepared using the glass beaker and stick.

Fig. 3
The amber glass container with adapter for oral syringe was used.

Conclusion and relevance

The formulation of tacrolimus was developed. Variety of concentrations of tacrolimus solution may be prepared. This allows us to prepare solution with higher concentration with the same volume, if needed. Our MTVx patient had a good tolerance to this solution. He has taken this solution since November 2021 and has remained stable without rejection of transplanted stomach, liver and pancreas.

It is necessary to work fast, because of an air flow in BSC, the ethanol evaporates and the solution may precipitate. Clinical effectiveness might be investigated to confirm the utility of this formulation.