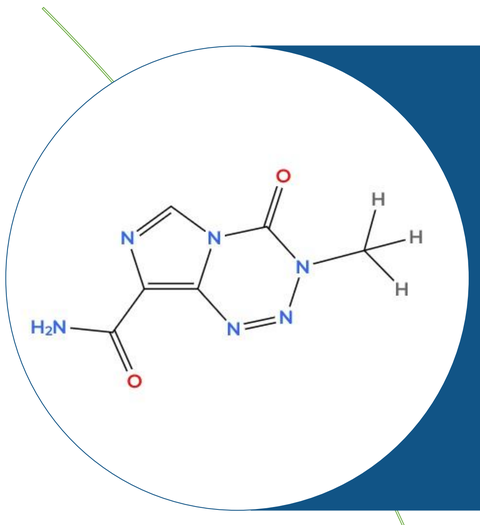
NOVEL METHOD OF COMPOUNDING AN ORAL TEMOZOLOMIDE SUSPENSION FOR PAEDIATRIC CANCER PATIENTS

M. Krauss*[1], K. Kussmann*[1], G. Ratzinger-Stöger[1], G. Stemer[1]
*contributed equally, [1]Pharmacy Service, University Hospital of Vienna, Austria



Background and importance

Temozolmide (TMZ) is a chemotherapeutic drug used to treat paediatric patients with neuroblastoma or solid brain tumors. Although TMZ is frequently prescribed for very young children, worldwide only hard capsules are available for oral treatment. Swallowing capsules is often not possible for young children and opening of the capsules is not recommended by the marketing authorization holder. However, based on literature[2], capsules might be opened and mixed with applesauce/acidic juice or processed into an oral suspension. This approach poses a risk to health care workers and/or relatives preparing the drug when not working in an isolator.

Aim and objectives

An oral TMZ suspension was developed, based on published literature and prepared using a novel compounding method. Commonly available capsules were processed with a wet mill to create a liquid preparation suitable for children.

Materials and methods

After a comprehensive literature search[3], a modified TMZ suspension 20mg/ml was prepared using a wet mill (WetMill Compact, FagronLab™)[4]. This device can process whole tablets and hard capsules in a closed system without having to grind or open them first. TMZ hard capsules were placed in the WetMill bottle together with preserved water (0,14% potassium sorbate), povidone K 25, sucralose and a strawberry flavour and wet-milled for 46 minutes. Syrspend® SF pH4 powder was added after the milling process, as wet-milling is more effective in low-viscosity media. Finally, the suspension was shaken vigorously.

Results

The visual inspection revealed a homogeneous suspension that could be applied directly from the WetMill bottle. Considering the modified TMZ formulation and lack of additional stability data, shelf life of the final product was limited to 2 weeks at 2-8 °C. The suspension can be administered via naso-gastric tube or orally. No handling problems or palatability issues were reported.

Conclusion and relevance

This new compounding method enables the safe production of liquid dosage forms of anti-cancer drugs or other carcinogenic, mutagenic or toxic drugs and represents a further step towards individualised treatment approaches. Suspension formulations for other antiviral and cytostatic drugs are in development.

making the difference in medication

[2] De Sio et al. (2006). *Temozolomide in resistant or relapsed pediatric solid tumors. Pediatric Blood & Cancer, 47(1), 30–36.* doi:10.1002/pbc.20516
[3]Annereau et al. Development of a Hospital Compounded, Taste-Masked, Temozolomide Oral Suspension and 5-Year Real-Life Experience in Treating Paediatric Patients. Pharmaceuticals 2022, 15, 555. https://doi.org/10.3390/ph15050555
[4]https://fagron.de/neu-fagronlab-wetmill-compact-nassmahlsystem/

3PC-044