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PURPOSE
Oral soluble film (OSF) is a thin film to be placed on the tongue, hydrated by saliva and quickly dissolve and release the active substance in the mouth for rapid absorption and action. It has emerged as a superior alternative for non-compliant patients (e.g., pediatrics, geriatrics or when nausea and vomiting episodes are frequent). For example, Clobazam OSF received FDA approval in 2018 for LGS (Lennox-Gastaut Syndrome) associated seizures. OSFs are also popular in pain relief or in the case of patients with opioid dependence, having lower abuse potential. Typical examples include Suboxone®, Belbuca®, Bunavail® and Onsolis®. Manufacturing of such products is based on techniques like melt-extrusion or film casting followed by damping, quality control and evaluation for disintegration and dissolution. Major downsides to the use of current USP dissolution methods (Apparatuses I, II, 3 and 4) or their modified versions include:

- Dissolution rate strongly dependent on agitation speeds and film positioning,
- Large hold-up volume lead to the loss of discriminatory role
- Rapid film breakdown and low residence time
- Poor reproducibility and inter-laboratory variations

The purpose of this study is to establish a dissolution method which can more realistically simulate the oral milieu, and more reliably and predictably determine the in vitro drug release from OSF.

METHOD
The melatonin OSF are prepared by the solvent casting method. In this method, the polymers (PEO WSRN-80, Carbopol) are premixed and dissolved in water. All the other excipients such as mannitol, citric acid are dissolved separately. Then the above solutions are mixed thoroughly and cast as a film on glass plate and allowed to dry in the 45°C oven, which is then cut into 1.5 cm x 1.5 cm pieces in three levels of dose: 3mg, 5mg, and 10mg. Dissolution is performed with the USP II paddle method at the speed of 50 rpm and 100 rpm using a Varian VX 7010 dissolution system. 500mL of simulated saliva at the pH of 6.7 is used as dissolution medium. The films are placed onto the mesh by tape as shown in Fig. 1a. Another innovative dissolution set up is illustrated in Fig. 1b. 20mL simulated saliva solution is used in the dissolution tube. The oral film is placed inside the basket to allow release from both sides of the film mimicking the in-vivo environment in the oral cavity. The film floatation was prohibited as it adhered to the basket wall and tube-basket assembly was shaken rather than rotating. The dissolution set up was put in the MaxQ 2000 shaker at 25 rpm to mimic the tongue movement. The sample solution (2uL) is then withdrawn at appropriate time intervals for UV/Vis analysis by Nanodrop 2000 at a determined time interval.

RESULT

CONCLUSION

- The novel dissolution method developed (Basket in tube) appears to mimic the oral cavity to a greater extent when compared to USP methods in terms of media volume, full film exposure and hydrodynamics which more closely resembles tongue masticatory movements.
- As a result a more predictable release profiles with least variations among the data were apparent and method can differentiate differences among films of different drug loadings. The basket in tube method has been designed with the idea to reproduce the tangential flow to mimic the tongue masticatory movements and low hold-up volume to mimic saliva volume secreted under normal condition and environment of the oral cavity.
- The small scale geometry of the method provides possibility for data collection every minute during the fast dissolving process.
- Basket in tube method is a discriminatory and reproducible method which shows excellent reliability for the evaluation of oral soluble films.

REFERENCE