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Short communication

Effect of high-shear mixer head on optical properties and disintegration time of orodispersible films

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Introduction

Although solid oral dosage forms present majority of commonly prescribed drugs, some patients struggle with ingesting them (Awad et al., 2021). Amongst those, a very significant group is the pediatric population. On the other side, questions concerning dosage consistency arise when it comes to liquid oral preparations, particularly for suspensions (Gupta et al., 2021).

To avoid the limitations of conventional oral dosage forms, orodispersible films (ODFs) were developed as a promising, patient-tailored therapeutic alternative. After the administration, ODFs are swallowed naturally with saliva, and there is no need for additional water (Yadav et al., 2021). Furthermore, in terms of the pediatric population, the product not only has to be easy to swallow, but it also has to be visually appealing. Therefore, a lot of attention is dedicated to the visual appearance of ODFs, including their color and transparency or opacity (Zamanian et al., 2021).

One of the methods used to produce ODFs is the solvent casting of polymer solution/dispersion. The aim of our study was to determine whether high shear mixer heads have an influence on the optical characteristics and disintegration time of the obtained ODFs.

Materials and methods

Sodium carboxymethylcellulose (Na-CMC) (TCI-Tokyo Chemical Industry Co., Ltd., Japan) were kindly provided by HARKE Pharma GmbH (Germany) and glycerin was ordered from Centrohem (Serbia).

Formulations containing 2% w/w Na-CMC and 1% w/w glycerin in distilled water were mixed with Silverson L5M-A high shear mixer (Silverson Machines Ltd., England) at 7000 rpm for 5 minutes (in accordance with our preliminary tests – data not shown). Three different mixer heads presented in Fig. 1 were used.

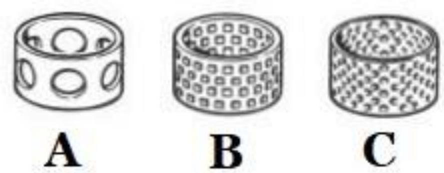

Fig. 1. High shear mixer heads: A) General purpose disintegrating head; B) Square hole high shear screen; C) Emulsor screen

The prepared solutions were poured into Petri dishes (diameter 90 mm) and dried for two days at room temperature. The dried films were then cut to the desired size (2 × 2 cm) and removed from the Petri dish.

Thickness of ODFs was measured using digital micrometer (Mitutoyo Co. Ltd., Japan) with 0.001 mm resolution. The measurements were made at three random positions and averaged to determine mean thickness.

The ODFs were fixed on the internal side of the cuvette and absorbance and percent transmittance (%T) were measured using UV-VIS spectrophotometer Shimadzu UV-1601 (Shimadzu Corporation, Japan) at 600 nm with air as blank. Transparency and opacity of ODFs were calculated using equations [1] and [2], respectively (Zhao et al., 2022).

Transparency=(log%T)/x [1]

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$$\text{Opacity}=A_{600}/x \quad [2]$$

Where %T is percent transmittance of light, A_{600} is absorbance of light and x is the thickness of ODFs.

Each measurement was performed in triplicate.

Three 2 × 2 cm ODFs were placed in Petri dishes, followed by the addition of 2 ml of distilled water. The Petri dishes were shaken constantly to allow water to rinse over the film. The time at which the film totally disintegrated was noted.

The collected data were analyzed with one-way analysis of variance (ANOVA) followed by Tukey's difference test as post-hoc test and presented as mean values ± standard deviations (SD).

Results and discussion

The results of performed tests for prepared ODFs are presented in Table 1.

Table 1. Characteristics of ODFs (mean ± SD; n = 3)

	ODF-A	ODF-B	ODF-C
Thickness (mm)	0.045± 0.001	0.040± 0.000	0.024± 0.002
%T	82.86±1.31	83.23±0.68	78.41±1.40
Transparency	42.32±0.15	48.01±0.09	77.85±0.32
Opacity (%)	1.79±0.15	1.98±0.09	4.34±0.34
Disintegration time (sec)	12.01±0.65	17.96±1.22	34.33±1.53

ODF-A is obtained with high shear mixer head A, which is used for mixing or disintegration of solids, while head B (ODF-B) is used for emulsion and fine colloid dispersion preparation. Head C is used for liquid/liquid and emulsion preparation. The effect of all three heads on ODFs characteristics is tested, as film comprises two liquids and one solid substance.

The results in Table 1 indicate that there is no significant difference in %T between ODF-A and ODF-B ($p>0.05$). On the other hand, the same parameter for ODF-C differs significantly ($p<0.05$). This could be because head C has the smallest orifice diameter and is generally used for emulsion preparation. As is known from the literature, lower transparency corresponds to greater opacity. Besides, it has been proven that the opacity and compactness of polymer films increase as the intermolecular forces between polymer and glycerin increase (Sharma et al., 2020). As the opacity and disintegration time of ODF-C are significantly greater ($p<0.05$) than those of ODF-A and ODF-B, it could be presumed that head C can lead to the formation of a more compact film matrix. It is not excluded that nanoscale particles can be obtained by using head C, as it is known that the presence of nanoparticles within the polymeric membranes can lead to a reduction in transparency (Zamanian et al., 2021). But this would need further evaluation for confirmation, and it exceeds the limitations of this manuscript.

Conclusion

According to the obtained results it can be concluded that the configuration of mixing equipment can significantly affect the optical characteristics and disintegration time of ODFs. Therefore, it would be extremely important to precisely establish in-process parameters during the ODFs’ development and manufacture.

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