

# Preformulation study of a new dosage form for Parkinson's disease: Orally disintegrating film of ropinirole hydrochloride

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## Introduction

Parkinson's disease (PD) is a disease characterized by a decrease in dopamine levels due to the loss of cells that produce a substance called dopamine, which allows brain cells to communicate with each other (Simon et al., 2020).

One of the most crucial dopamine receptor agonists, ropinirole hydrochloride (ROP), is an active ingredient used not only in PD but also in restless legs syndrome, which includes symptoms such as burning, numbness, tremor, tingling, pain, cramping or spasms. ROP is a Class III drug according to the Biopharmaceutical Classification System (BCS) due to its high solubility and low permeability.

Orally disintegrating films (ODFs) have attracted a lot of attention in recent years because it provides an immediate effect after rapid dissolution, are easy to prepare, and offer ease of use for patients such as children and the elderly (Patil and Shrivastava, 2014).

The aim of this study is the preparation of new dosage forms compared to the commercial product containing ROP, which is used in the treatment of PD and has limitations in use in geriatric patients due to difficulty in swallowing.

## Materials and methods

Firstly, the melting point determination, X-ray powder diffraction (XRD) analysis, and Fourier-transformed infrared (FTIR) analysis were performed for the purity analysis of the active substance ROP. The compatibility study of the formulation components used in the preparation of ROP ODFs was conducted by FTIR.

Electrospun ODF formulations of ROP were prepared according to Table 1. ROP ratio was 0.5% (w/w) for all formulations. Polyvinyl alcohol (PVA) as polymer at different concentration of 10% and 15%, propylene glycol (PG), and polyethyleneglycol 400 (PEG 400) as plasticizers at same concentration of 10% were used in the formulation. After ODFs are taken on the tongue, citric acid was used to provide salivary stimulation, sodium lauryl sulfate as a surfactant, and mannitol to flavor the formulation. Formulation components were dissolved in distilled water and the nanofibers were obtained by a flow rate of 1.5 mL/h, collector rotation speed of 200 rpm, nozzle between collector with a distance of 17 cm, and an applied voltage of 18.5 kV.

Morphological and organoleptic controls of ROP-ODFs were analyzed by optical microscopy and scanning electron microscopy (SEM). Disintegration times in distilled water and artificial saliva (with pH 6.75) were investigated. Also, surface pH measurement was made in ROP ODFs with Mettler Toledo Seven Compact®.

## Results and discussion

Melting point study of pure ROP was made with the Stuart SMP10 model and it was found to be 251 °C.

In the data of ROP in DrugBank Online, the melting point is stated between 243 - 250 °C, and the result of the study was found to be similar to DrugBank.

FTIR and XRD results of ROP were found to be similar to PubChem and literature (Dudhipala and Gorre, 2020).

The drug-excipient compatibility studies using FTIR were carried out with physical mixture 1 containing

Ropinirole, PVA, PG, citric acid, SLS, mannitol, and physical mixture 2 containing ropinirole, PVA, PEG 400, citric acid, SLS, mannitol. According to the FTIR result, no incompatibility was found between the active substance and the excipients.

Table 1. ROP-ODF formulation parameters

	PVA ratio (%)	PG ratio (%)	PEG 400 ratio (%)	Citric acid ratio (%)	SLS ratio (%)	Mannitol ratio (%)
DF1	10	10	-	2	1	2
ODF2	15	10	-	2	1	2
ODF3	10	-	10	2	1	2
ODF4	15	-	10	2	1	2

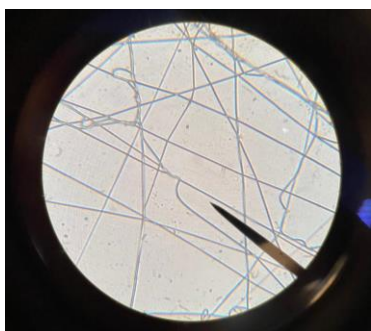


Fig. 1. Optical microscopy image of ODF3

Morphological and optical evaluations revealed that ODFs had a flexible and smooth structure. In Figure 1, it is shown that the fibers are homogeneously and regularly distributed in the optical microscope image of the ODF3-coded formulation.

The disintegration time of ODFs within 2 cm x 2 cm dimensions in 10 mL distilled water was measured as 2 s for ODF1, 3 s for ODF2, 3 s for ODF3, and 3 s for ODF4, respectively. Also, the disintegration time of ODFs within 2 cm x 2 cm dimensions in 10 mL artificial saliva was measured as 3 s for ODF1, 2 s for ODF2, 2 s for ODF3, and 2 s for ODF4, respectively.

The pH measurement results of ODFs were found as 7.075 for ODF1, 7.173 for ODF2, 7.384 for ODF3, and 7.415 for ODF4, respectively.

## Conclusion

Preformulation studies for ROP ODF have been carried out successfully. Rapid disintegration was observed in the mouth with a disintegration time of 2-3 seconds in all ODF formulation.

All polymer ratios were found to be suitable for the electrospinning process. Polymer type, polymer ratio, and plasticizer type directly affected the properties of ROP ODF nanofibers.

Electrospun ODFs could be a potential drug delivery system for the treatment of PD for ropinirole hydrochloride.

## References

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