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# ABSTRACT BOOK

# P-08
# DICLOFENAC SODIUM LOADED RESOMER® RG 502 H NANOPARTICLES FOR ORAL APPLICATION: FORMULATION AND *IN VITRO* CHARACTERIZATION

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## 1. INTRODUCTION

Diclofenac sodium (DS) is a non-steroid anti-inflammatory drug (NSAID) and is the most prescribed for the treatment of pain and inflammatory diseases. Like all NSAIDs, DS exerts its effects by inhibiting prostaglandin synthesis by blocking COX-1 and COX-2 enzymes [1, 2]. Indications for use include rheumatic disease, migraine, musculoskeletal and postoperative pain. It is also used for actinic keratosis, peripheral and postoperative inflammation and ophthalmic seasonal allergic conjunctivitis. It has been associated with opioid protective effects in the treatment of cancer pain. DS is very well absorbed orally, binds to plasma proteins at almost entirely therapeutic levels and has a half-life of about 1-2 hours [1]. Nanoparticles (NP's) are being extensively investigated as drug delivery systems for pharmaceutical applications. The most commonly used biodegradable polymers in the production of NP's for modified release are polyglycolic acid, polylactic acid and their copolymers, e.g., PLGA (polylactic-co-glycolic acid) [3]. In this study, DS loaded NP's with modified release profiles are prepared by 'Double Emulsification Solvent Evaporation Technique' and their *In Vitro* characteristic properties are evaluated.

## 2. MATERIALS AND METHODS

### 2.1. Materials

Diclofenac sodium is a kind gift from Abdi İbrahim (Istanbul, Turkey). Poly(lactic-co- glycolic acid) (PLGA) (Resomer® RG 502 H) and polyvinyl alcohol (PVA) were obtained from Sigma (Germany). All other chemicals used were of analytical grade.

### 2.2. Preparation of nanoparticles

The NP's were prepared by 'Double Emulsification Solvent Evaporation Technique'. Weighed amount of PLGA (60 mg) was dissolved in acetone (3 mL). Then, 400 µL aqueous solution of PVA (0.5 % w/v) was added drop-wise to 3 mL PLGA solution using ultrasonic bath (1 minute, Wisd Laboratory Instruments, WUC-A03H, Korea) (W1/O). 3 mL of this emulsion was then added drop-wise to 10 mL of PVA aqueous solution (0.5 %, w/v) under probe sonicator (5 min, 50% amplitude, Sonics®, USA) (W1/O/W2). The acetone was evaporated at room temperature in 4 hours to obtain an aqueous dispersion which was finally centrifuged to obtain the NP's (Rotina 420R, Hettich Zentrifugen, Germany). After washing twice, the NP's were resuspended in the distilled water and then frozen in freezer and lyophilized (Scanvac CoolSafePro Labogene, Denmark) to obtain a fine powder. For the preparation of DS-loaded NP's, the procedure started by adding different amount DS to 400 µL PVA aqueous solution (0.5 % w/v). All remaining procedures are as previously described. Formulation contents are presented in Table 1.

**Table 1.** formulation contents

| Code | PLGA (Resomer® RG 502H) | Diclofenac Sodium |
|---|---|---|
| Blank | 60 mg | - |
| NP-1 | 60 mg | 3 mg |
| NP-2 | 60 mg | 6 mg |
| NP-3 | 60 mg | 9 mg |

### 2.3. Characterization of nanoparticles

Zetasizer Nano ZS (Malvern Instruments, UK) was used to analyze particle size (PS), polydispersity index (PDI) and zeta potential (ZP) of NP's. The entrapment efficiency and release study of NP's were performed with UV-vis spectrophotometer (Shimadzu UV-160A, Japan) and the detection wavelength is 276 nm. Entrapment efficiency was expressed as 'EE %' following Equation 1 (Eq. 1)

$$EE\ \% = \left[\frac{\text{Actual amount of DS loaded in PLGA NP's}}{\text{Theoretical amount of DS oaded in PLGA NP's}}\right] x100 \qquad \text{Eq.1}$$

*In vitro* release study of the formulations was investigated over 24 hours and performed in simulated intestinal fluid (SIF, pH 6.8).

## 3. RESULTS AND DISCUSSION

### 3.1. Characterization of nanoparticles

PS, PDI, ZP and EE % values of NP's are shown in Table 2. *In vitro* release profile of DS and formulations are shown in Fig. 2.

**Table 2.** PS, PDI, ZP and EE % results

| Code | PS | PDI | ZP | EE % |
|---|---|---|---|---|
| Blank | 106.4±4.9 | 0.135±0.021 | -17.9±3.0 | - |
| NP-1 | 114.7±1.4 | 0.113±0.084 | -17.8±1.7 | 77.82±4.38 |
| NP-2 | 119.7±0.5 | 0.147±0.043 | -19.9±1.2 | 52.87±1.16 |
| NP-3 | 124.8±1.0 | 0.136±0.013 | -19.8±0.3 | 41.44±6.02 |

Nanosized particles determined with 114.7-119.7 nm sizes can be attributed to the hydrophobicity of the polymer used [3]. The NP-3 coded NP formulation appeared to have bigger sizes when compared to other DS-loaded particles. PDI distribution in a given system, reflects the quality of the NP dispersion within the range of 0.0–1.0. PDI values ≤0.1 indicate the highest quality of dispersion. Most researchers recognize PDI values ≤0.3 as optimum values; however, values ≤0.5 are also acceptable [4]. According to this literature, quality and monodisperse NP's have been prepared. The negative ZP is thought to be due to carboxyl end groups of PLGA [5]. As a result, formulations with a high EE % were produced and the EE % was decreased by increasing the amount of agent. The release of DS from NP's continued over 24 hours while pure DS exhibited a rapid release of 96.35 % in 1 hour. When the DS release from all NP formulations was examined, it was found to be sustained release after the explosion effect in the first 6 hours.

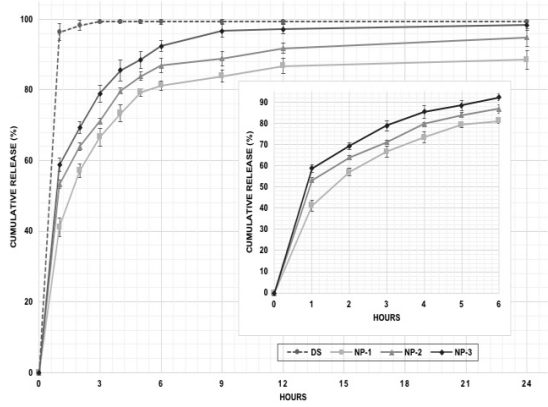


**Figure 2.** Release profile of KT and formulations

## 4. CONCLUSION

In this study, NP's were prepared with PLGA. We have successfully formulated, DS loaded NP's by double emulsification solvent evaporation technique. It could be concluded that DS loaded NP's seem to be a promising delivery system for the oral application according to the results such as PS, PDI, ZP, EE% and release rates.

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