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Review Article

Processing temperature impacts on the drug release from the polymeric micro/nanoparticles

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ABSTRACT

Polymeric micro/nano-particles have become an invaluable tool as a novel drug delivery systems, and due to the sensitivity of the polymeric matrix to any thermal treatment, the processing temperature should be given a great deal of attention together with the interrelated specific polymer own polymer characteristics, such as polymer glass transition temperature and crystallinity. This review is an attempt to shed the light on the impact of the processing temperature on the drug release kinetics from polymeric micro/nanoparticles.

Keywords: Drug delivery systems, Micro-particles, Nanoparticles, Polymers, Temperature

INTRODUCTION

Recently, researches have focused on polymeric micro-spheres as drug delivery systems, due to its characteristics like the ease of administration through the different routes (oral, systemic.,), in addition to the ability to be tailored for desired release profiles,[1] and polymers have a specific thermal identity characteristic or indicator that should be considered at any heat processing step of the polymer or the polymeric system,[2] which is called glass transition temperature, Tg, that gives the ability to clarify various aspects of drug release kinetics from polymeric micro-spheres,[3] at the glass transition temperature Tg, an amorphous polymer softens, and transforms from a glassy state to a rubbery one due to increased segmental mobility,[4] and these transformations can be thermodynamically measured using a technique that is known as differential scanning calorimetry.[5]

METHODOLOGY

A number of related articles were collected and screened and the most relevant to the subject were screened, and data were arranged in such a way to serve the purpose.

DISCUSSION

In an experimental study to verify the effect of temperature on the mechanisms of drug release from poly(lactic-co-glycolic) acid (PLGA) micro-spheres, Izumikawa *et al.* reported that release rate of progesterone from these micro-spheres was higher when the temperature was elevated above the glass transition temperature Tg,[6] the thing that refers to the correlation between the

crystallinity of the polymer and the trapped drug release mechanisms which also complies with what Izumikawa *et al*. found, that the progesterone release from PLGA micro-spheres from the crystalline polymer matrices exhibited a rapid drug release, while micro-spheres of amorphous polymer matrices provided a slower drug release rate.[7]

Miyazaki *et al*., in a study on theophylline release from a hydrophobic dextran, found that the drug release at the first 8 h was 28% at the processing temperature of 30°C, and 84% at 7.5°C with a different morphological characteristics between the two preparation temperature, that also highlight the effect of processing temperature on the drug release kinetics from the polymeric micro-spheres.[8] Yang *et al*. also reported that preparation temperature has significant effects on the release profile of biovine serum albumin from PLGA micro-spheres so that micro-spheres prepared at 33°C were found to give the highest initial burst release. However, micro-spheres fabricated at lower temperatures (5°C, 15°C, and 22°C) exhibited the same steady rates, and micro-spheres that prepared at higher temperatures gave very low release rates after their initial release.[9] Liu and McEnnis also indicated that glass transition temperature is an excellent indicator of drug release profiles and may be used in formulating a designed PLGA controlled drug release micro-particles,[10] Shi *et al*. found that the release rate of indomethacine from the Calcium Alginate/Poly(N-isopropylacrylamide) Beads was higher at 37°C than that at 25°C highlighting the effect of temperature on the drug release profile.[11]

Dubey *et al*. reported in a study about the effect of heating temperature and time on the pharmaceutical characteristics of albumin micro-spheres containing 5-fluorouracil, that the heating temperature and heating time may affect the drugs release in target tissue,[12] Zolnik *et al*. reported that dexamethasone-loaded PLGA micro-spheres release rate at 37°C was different from the release behaviors that are at a higher temperatures (45, 53, 60, and 70) °C, that was explained by the morphological changes at the elevated temperatures which resulted in a remarkable reduction in burst release.[13] Mooranian *et al*. reported also that the *in vitro* release of metformin from (sodium alginate/ Eudragit®RS30D) based micro-spheres at a temperature of 25°C and above, induced a direct impact on drug release and the stability profiles.[14]

Jeong *et al*. found that the crystalline microstructure has a direct impact on the papaverine release kinetics from poly(epsilon-caprolactone) (PCL) micro-spheres, the thing that was interpreted by the fact that the release rate is governed by the microstructure of PCL micro-particles, which in its role changes according to processing conditions such thermal history, highlighting the role of the processing temperature on the release profile from polymeric micro-particles,[15] and not far from these findings. Otte *et al.* found in a study about the impact of post-processing temperature on risperidone-loaded PLGA micro-particle properties, that the post-processing temperature affects several characteristics of the resultant micro-particles such as morphology, glass transition temperature, and drug loading, and these changes consequently affect the drug release rate.[16]

CONCLUSION

It is clear that the processing temperature has a significant impact on the release profile of the drug from the polymeric micro/nanoparticles, and the impact of any thermal treatment on the drug release kinetics from the polymeric micro/nanoparticles should be carefully investigated for each polymeric system, and a more deep comprehension of the effect of the phase transitions between the amorphous and crystalline states of the polymeric micro-particles on the drug release may open the door for a more precise and tailored release rates.

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