TRANSLATIONAL POTENTIAL OF MICROARRAY PATCHES CONTAINING AMOXICILLIN SODIUM: A PRIMARY PACKAGING STUDY

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Background: With the recent advances in microarray patch (MAP) technology and a potential move towards commercialisation of MAP products, there is a need to address issues surrounding the translation of MAP technology from the laboratory setting to that of the end-user. One important aspect of MAPs moving forward is appropriate primary packaging. This research focuses on amoxicillin (AMX)-containing MAPs. These MAPs are currently being explored for their potential role in the treatment of neonatal sepsis in humid and hot countries. In this work, a MAP consists of a hydrogel-forming microneedle (MN) and a drug-containing reservoir. Improper primary packaging in humid and hot countries may result in degradation of active drugs, with the use of substandard medicines a major health concern. AMX is inherently unstable, as hydrolysis readily occurs, due to the presence of a labile ß-lactam ring. The research presented here, seeks to investigate the effects of primary packaging on MAP integrity, MAP physical characteristics and AMX recovery from AMX-containing MAPs.

Methods: MNs were fabricated from aqueous blends containing 15% w/w poly(vinyl alcohol), 10% w/w poly(vinyl pyrrolidone) and 1.5% w/w citric acid. Using a manual hydraulic press, reservoirs were prepared using 95% w/w AMX and 5% w/w sodium starch glycolate. MAPs, MNs and reservoirs were then packaged and stored under accelerated storage conditions (40°C and 75% RH) for 168 days, in accordance with international guidelines. The control cohort was MAPs, MNs and reservoirs left unpackaged. At pre-defined intervals, the insertion capabilities of MNs were investigated, using a previously-validated skin simulant, Parafilm M®. Physical characterisation and AMX recovery from the reservoirs were also conducted.

Results: Major causes of drug instability are moisture and temperature. To avoid unnecessary degradation, two semi-impermeable primary packaging, in terms of a barrier to moisture and heat was sought. MAPs in Protect(470) foil demonstrated that measurable amounts of AMX didn't migrate into attached MNs. At all-time intervals tested, MNs packaged in Protect(470) foil could insert into 3 layers of Parafilm M®. For example, after 168 days of storage, 21.42 ± 6.80% holes were created in layer 3 of the skin simulant, which is consistent with results from previous studies. Reservoirs demonstrated uniform physical dimensions when packaged in Protect(470) foil. This wasn't the case for reservoirs packaged in Poly(ester) foil. After 168 days, the % of AMX recovered from reservoirs packaged in Protect(470) foil was 103.51 ± 7.03%. However, packaged in Poly(ester) foil, the AMX content significantly (p<0.0001) decreased, which is likely due to the degradation of AMX by the imbibed moisture.

Conclusions: Primary packaging is imperative in maintaining the efficacy and stability of labile medicines and MAPs. For the first time, this study evaluates AMX-containing MAPs in different primary packaging. Of the two different types of primary packaging investigated, the results are very promising for MAPs packaged in Protect(470) foil in terms of moisture barrier function and temperature resistance. This work indicates the importance of investigating the storage stability of other drug-containing MAPs, to ensure they are 'fit for purpose' when they reach the end-user.