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A Bilayer Hydrocortisone Matrix Tablet for Paediatric Biphasic Drug Delivery

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Background

Hydrocortisone (HCT) is widely used for glucocorticoid replacement and anti-inflammatory therapy and is the preferred treatment for adrenal insufficiency due to its similarity to endogenous cortisol. In paediatric patients, accurate dose administration is essential, as insufficient exposure may lead to adrenal crisis and poor disease control, whereas excessive exposure may impair growth. Conventional immediate-release (IR) formulations are limited by HCT's short half-life, rapid clearance, multiple daily dosing, and difficulties in dose adjustment for children (1-5).

Objectives

The aim of this study was to develop a bilayer HCT matrix tablet for paediatric use, combining an IR layer and a sustained-release (SR) layer to provide a total dose of 5 mg HCT. The IR layer was designed to deliver HCT rapidly, providing prompt glucocorticoid availability after administration, while the SR layer was formulated to release HCT in a controlled manner, aiming to prolong drug exposure and reduce fluctuations in plasma concentrations. This dual-release approach was intended to improve therapeutic performance by providing an initial rapid increase in hydrocortisone levels followed by sustained drug release, potentially reducing dosing frequency and better supporting physiological cortisol replacement requirements in paediatric patients.

The development of this biphasic delivery system represents an approach toward improving paediatric HCT therapy by combining rapid onset of action with prolonged release characteristics in a single dosage form, while maintaining dose accuracy and patient acceptability.

Methods

The tablets were prepared by accurately weighing HCT and the excipients, as shown in Table 1 using a high-precision analytical balance. The weighed ingredients were subsequently blended in a laboratory-scale powder blender (32 rpm, 8 min). The produced mixture was precisely weighed, filled to a 10 mm diameter dye, and directly compressed using a hydraulic press.

The release of HCT from each formulation was assessed using a USP II dissolution paddle apparatus at 50 rpm and a temperature of 37 ± 0.5 °C at pH 1.2 aqueous medium for the first 2 h, and at pH 6.8 aqueous medium for the next 6 h.

Results

The release profiles demonstrated that excipient composition had a significant impact on drug release from the bilayer formulations (Figure 1):

- Formulations F2 and F4, containing lower amounts of Compritol® 888 ATO and Celny VH in the SR layer combined with a higher drug load in the IR layer, exhibited faster and more extensive release, reaching approximately 75% and 93% drug release, respectively.
- In contrast, F1 and F3, which contained higher lipid and polymer contents in the SR layer, showed slower release, suggesting that the increased matrix-forming excipients created a stronger diffusion barrier.
- The enhanced release observed for F4 compared with F2 indicates that the higher IR drug loading further contributed to the initial burst while maintaining SR.
- Overall, the balance between the lipid matrix (Compritol® 888 ATO) and the hydrophilic polymer (Celny VH), together with drug distribution between the IR and SR layers, effectively modulated the release kinetics.

Table 1: Formulations F1-F5 composition

Immediate release layer				
Ingredient	**F1 (mg)**	**F2 (mg)**	**F3 (mg)**	**F4 (mg)**
HCT	2.00	3.00	2.00	3.00
StarLac	7.90	11.85	7.90	11.85
Magnesium Stearate	0.10	0.15	0.10	0.15
Sustained release layer				
Ingredient	**F1 (mg)**	**F2 (mg)**	**F3 (mg)**	**F4 (mg)**
HCT	3.00	2.00	3.00	2.00
Compritol 888 ATO	7.00	5.48	7.00	5.48
Celny VH	4.85	2.42	4.85	2.42
Magnesium Stearate	0.15	0.10	0.15	0.10

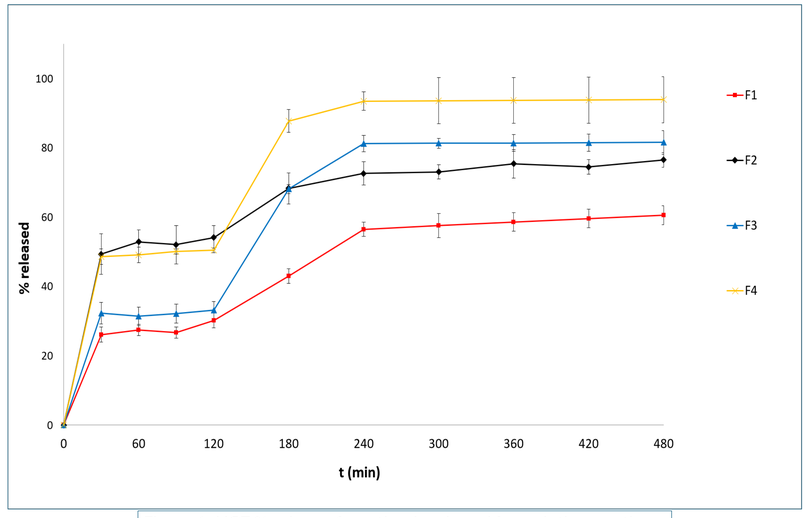


Figure 1: HCT % release from the developed formulations vs time

Conclusions

The developed bilayer HCT tablet successfully demonstrated a biphasic release profile, combining rapid initial drug availability with prolonged HCT release through optimized excipient composition and drug distribution. This formulation approach may provide a promising paediatric-friendly alternative for improving hydrocortisone replacement therapy by enhancing dosing flexibility and maintaining more consistent drug exposure.

References

1. Protopapa C.; Siamidi A.; Kolipaka S.S.; et al. (2024) In Vitro Profile of Hydrocortisone Release from Three-Dimensionally Printed Paediatric Mini-Tablets. Pharmaceutics 16(3):385.
2. Ranmal, S.R.; Cram, A.; Tuleu, C (2016). Age-appropriate and acceptable paediatric dosage forms: Insights into end-user perceptions, preferences and practices from the Children's Acceptability of Oral Formulations (CALF) Study. Int. J. Pharm. 514, 296–307
3. Conroy, S.; Sweis, D.; Planner, C.; et al. (2007). Interventions to reduce dosing errors in children: A systematic review of the literature. Drug Saf. 30, 1111–1125
4. Madathilethu, J.; Roberts, M.; Peak, M.; et al.(2018)Content uniformity of quartered hydrocortisone tablets in comparison with mini-tablets for paediatric dosing. BMJ Paediatr. Open, 2, e000198.
5. Speiser, P.W.; Arlt, W.; Auchus, R.J.; et al.(2018)Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: An endocrine society clinical practice guideline. J. Clin. Endocrinol. Metab., 103, 4043–88.