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Detectability of glucocorticosteroid formulations available in Indian market following different routes of administration

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Introduction

Glucocorticosteroids are very potent anti inflammatory substances. The use of LCMS-MS for the detection of glucocorticosteroids solved the problem of sensitivity and selectivity in their detection [1-5].In India use of glucocorticosteroids by various medical practitioners is wide spread for a genuine and not so genuine reason to treat various ailments. These are administered as available allopathic medicines and also as ayurvedic medicines spiked with corticosteroids. The aim of the present study is to detect various glucocorticosteroids preparations available in Indian market following different administration routes which might be used intentionally or sometimes inadvertently. The effect of these glucocorticosteroids on steroid profile and endogenous glucocorticosteroids is also studied.

Methodology

The study was approved by the local ethical committee. The study was performed in sixty two male volunteers in the age group of 25-35 years with weight and height 67.08±9.45 kgs and 174.96±5.51 cm, respectively. The volunteers were randomly divided into five groups which included oral (n=16), topical (n=16), injectable (n=6), inhaler (n=16) and placebo (n=8) groups. The testing was done by the method published earlier [6].

The oral preparations betamethasone (1 mg/day) and prednisolone (5 mg/day) are given for ten days. Urine samples are collected during ten days of administration at 3 hrs interval and for ten days post administration at 12 hrs interval. The topical and inhalers are given in a single dose and urine sample collected at 3 hr interval for 48 hrs. Similarly a single dose of triamcinolone (40mg) intramuscular injection was given and urine samples are collected for eight days post administration at 12 hrs interval. The effects of all these glucocorticosteroids

on endogenous glucocorticosteroids (hydrocortisone (HS), cortisone (CS), tetrahydrocortisone (THCSE) and tetrahydrocortisol (THCSL)) were also studied.

Results & Discussion

Topical Preparations: The dermatological application of fluticasone propionate could not be detected in urine after applying one gram of ointment in between the buttocks whereas beclomethasone could be detected (0.4 ng/mL) in traces at 24 hrs of application.

Inhalator preparation: Beclomethasone (3.9 ± 0.97 ng/mL) and budesonide (6.53 ± 0.02 ng/mL) could be detected till 24 hrs of administration which was much below MRPL (Fig 1a).

Oral Preparation: Betamethasone levels during the ten days administration ranged from 1.4 ± 2.0 ng/mL to 58.2 ± 13.9 ng/mL and could not detected in post treatment (Fig 2b). The prednisolone was found in 280 ng/mL during first day of administration and could be detected in urine nine days post administration in the range of 33.3 ± 8.4 to 37.8 ± 9.4 ng/mL. The 20-dihydro prednisolone (20-β-hydroxy) could also be detected up to ten days post treatment (Fig 1c). The four different oral ayurvedic preparations which were given to the patients suffering from backache were tested and two of the four preparations showed presence of beta/dexamethasone at MRPL. However, the urine sample of the patient did not show presence of beta/dexamethasone on day1. After three days of treatment the urine sample of the patient showed presence of beta/dexamethasone (Fig 2a).

Intramuscular preparation:

The triamcinolone acetonide after single intramuscular injection could be detected till eight days .The level of triamcinolone on 8^{th} day was 8.4 ng/mL (Fig 2b).

Effect of corticosteroid on endogenous corticosteroids:

The effect of all these corticosteroids on endogenous corticosteroids was also studied (Fig 3a, b, c). Topical application of fluticasone showed decrease in cortisol at 24 hrs of application. The beclomethasone inhaler group showed suppression of cortisol, cortisone and tetrahydrocortisone whereas budesonide did not show any suppression of endogenous corticosteroids. The triamcinolone acetonide (Injection) showed suppression in all endogenous corticosteroids at 24hrs of application.

Conclusion

The aim of the study to detect various corticosteroids available in Indian market could be achieved. It is suggested that medical practitioners and athletes should be aware of the possibility of testing positive with the use of ointment /inhaler /ayurvedic medicines which may otherwise be considered safe for use. Further, the medical fraternity in India needs to be

advised to use oral and Injectable corticosteroids more judiciously rather than using as a magic drug for fast recovery. The suppression of various endogenous corticosteroids with the use of synthetic corticosteroids may be due to negative feed back mechanism. This needs to be studied in details with the reference ranges of endogenous corticosteroids.

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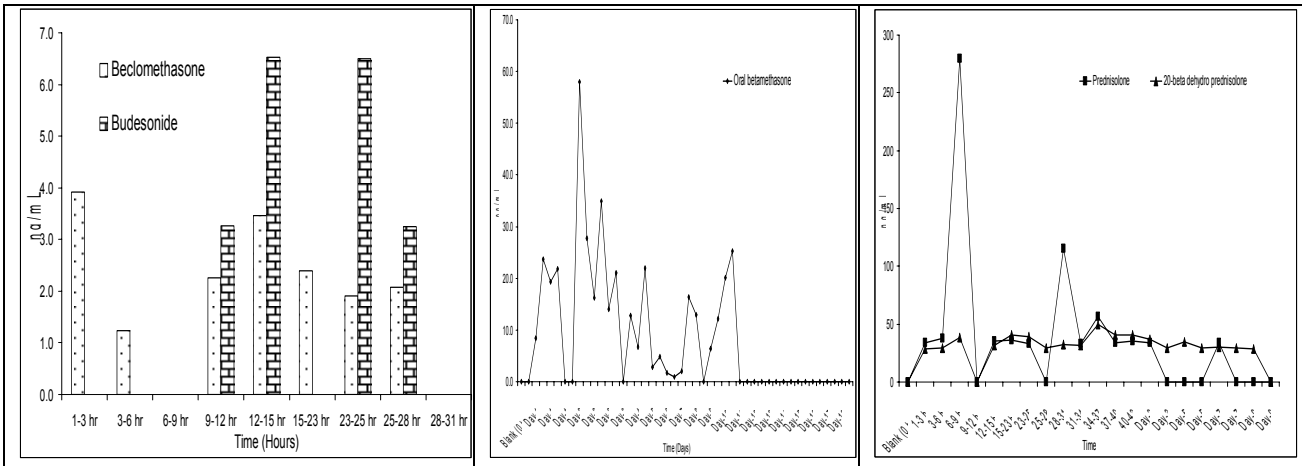
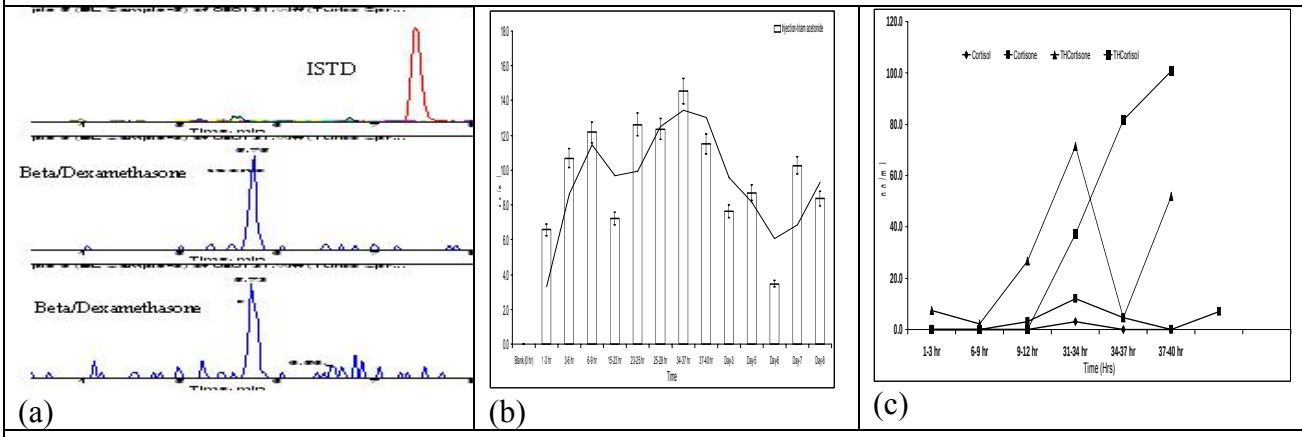


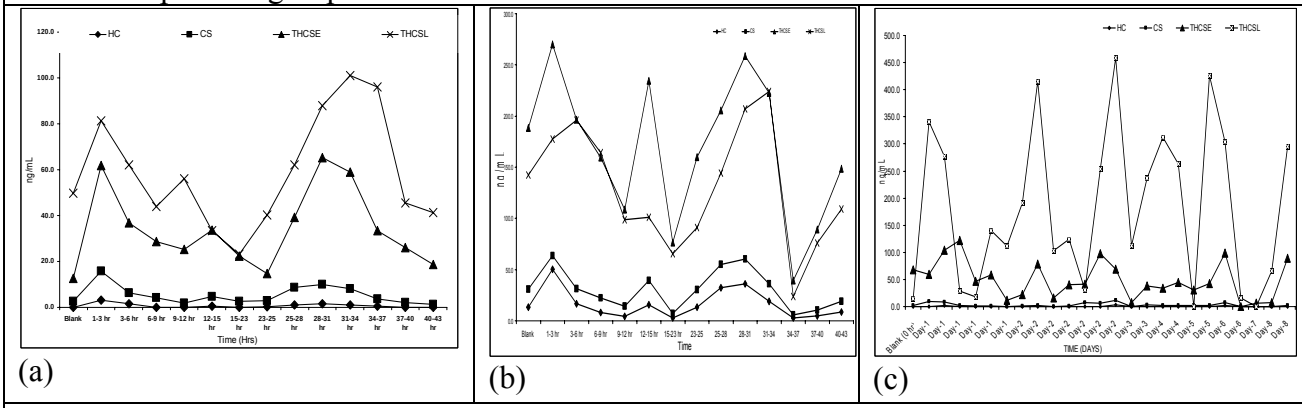
(a) (b) (c)

Figure 1 Urinary concentrations of (a) beclomethasone dipropionate & budesonide after inhalation of one puff (200 mcg/puff) (b) betamethasone (oral-1mg of Betnesol™) (c) Prednisolone & 20-dihydro prednisolone (oral -5 mg Wysolone™)



(a) (b) (c)

Figure 2 Urinary concentrations of (a) Beta/dexamethasone (oral administration-ayurvedic preparation) (b) Triamcinolone (intramuscular administration-40mg) (c) HC, CS, THCSE and THCSL in placebo group



(a) (b) (c)

Figure 3 Urinary concentration of HC,CS,THSCE and THCSL after (a) dermatological application of Fluticasone propionate (b) inhalation of beclomethasone propionate (c) Triamcinolone injection