Adrenocorticoids

Introduction

The adrenal gland secretes numerous steroids of which aldosterone and hydrocortisone are the major ones. The structures of aldosterone and hydrocortisone are

![Cortisol](image1)
![Aldosterone](image2)

The steroids secreted are called adrenocorticoids. Aldosterone possesses mineralocorticoid activity while hydrocortisone is a glucocorticoid.

Mineralocorticoid activity is related to retaining salt, NaCl. Mineralocorticoids maintain electrolyte balance by retaining Na+ and promoting K+ excretion.

Glucocorticoids have numerous physiological activity. They are important for the biosynthesis and metabolism of carbohydrates, proteins and lipids. They are also involved in immune responses. This statement itself suggests the phenomenal importance of these drugs. In addition, glucocorticoids possess anti-inflammatory activity. This activity has become so important that we now refer to only the anti-inflammatory activity of glucocorticoids and conveniently forget the systemic action of these hormones.

Adrenocorticoids are used in:

- Addison’s disease: decreased production of adrenocorticoids e.g., in TB
- Adrenalectomy: elimination of adrenal cortex
- Cushing’s syndrome: hyperadrenalism e.g., tumors

Decreased production of adrenocorticoids leads to reduction in resistance to trauma, increased sensitivity to pain.
Biochemical Mechanism of Action

Anti-inflammatory Activity of Glucocorticoids

Cortisol induces the production of lipocortin and related proteins by increasing gene expression through the glucocorticoid receptor mechanism. Lipocortin inhibits the activity of phospholipase A2 which liberates arachidonic acids and leads to the production of eicosanoids/prostaglandins and leucotrienes which are the mediators of inflammation. Because glucocorticoids have systemic activity they are not used as systemic anti-inflammatory drugs. Hence we find these primarily in topical applications such as creams and ointments.

Mineralocorticoid activity
The mineralocorticoid action of these steroidal hormones relates to synthesis of aldosterone – induced protein which is a permease that regulates cell permeability to Na+ and maintain Na+ influx (elevated Na+-K+-ATPase Pump).

**Structure-Activity Relationships**

The structure of glucocorticoids determine their biological activity. Innumerable molecules have been studied to reduce the mineralocorticoid activity and retain the glucocorticoid activity. Some drugs that are currently available in the market are:

- cortisol
- fludrocortisone
- 11-deoxycorticosterone
- prednisolone, 6α-methyl prednisolone
- betamethasone
- dexamethasone
Based on these and other studies we can generalize the following guidelines for anti-inflammatory activity of glucocorticoids:

1. All trans steroid skeleton is required for anti-inflammatory activity
2. Presence of $\Delta^4$-3-keto, 11$\beta$-OH, 17$\beta$-OH needed for anti-inflammatory activity
3. Planarity of A ring without losing 19-CH$_3$ group for anti-inflammatory activity
4. Substitution of 9$\alpha$,6$\alpha$, 16$\alpha$- favor anti-inflammatory activity in most cases
5. F>Cl>Br>I for anti-inflammatory activity