DETERMINATION OF MORPHOFUNCTIONAL CHANGES IN THE ADRENAL GLAND UNDER HYPOXIC CONDITIONS AND EVALUATION OF THEIR CORRECTION MECHANISMS USING EUPHORBIA LATHYRIS EXTRACT

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Abstract. *Hypoxia is a fundamental pathophysiological state that disturbs cellular energy metabolism and the secretory activity of the endocrine glands, among which the adrenal gland is one of the most sensitive owing to its high metabolic rate and rich blood supply. This article reviews and characterises the morphofunctional changes occurring in the layers of the adrenal gland under hypoxic conditions and evaluates the corrective potential of an extract of caper spurge (Euphorbia lathyris). Under sustained oxygen deficiency the cortical zones undergo degenerative ultrastructural changes — vacuolation, mitochondrial swelling, condensation of nuclear chromatin and lipid accumulation — accompanied by reduced proliferative activity and intensified apoptosis. Treatment with Euphorbia lathyris extract, rich in flavonoids, triterpenoids, polyphenols and alkaloids, restored mitochondrial structure, normalised oxidative phosphorylation, lowered lipid peroxidation and improved microcirculation, with morphometric parameters and the expression of proliferative (Ki-67) and anti-apoptotic (Bcl-2) markers approaching normal values. The findings indicate that Euphorbia lathyris extract is a promising phytotherapeutic agent for correcting hypoxia-induced endocrine dysfunction.*

Keywords: *adrenal gland, hypoxia, morphofunctional changes, Euphorbia lathyris, antioxidant, apoptosis, Ki-67, Bcl-2, phytotherapy.*

Introduction

The adrenal glands are among the most important endocrine organs of the human body, playing a decisive role in adaptation to stress, the maintenance of homeostasis, and the regulation of water–salt and energy metabolism. Each gland consists of a cortex and a medulla, which together govern the neuroendocrine system through the secretion of distinct hormones. The cortex is organised into three zones: the zona glomerulosa, which produces mineralocorticoids; the zona fasciculata, which produces glucocorticoids; and the zona reticularis, which produces sex hormones. The medulla, in turn, ensures the synthesis of the catecholamines adrenaline and noradrenaline.

In the healthy gland, hormone synthesis and cellular morphology operate in close harmony. Histologically, the boundaries between the zones are distinct, the parenchymal cells are polygonal, the nuclear–cytoplasmic ratio is balanced, and an extensive capillary network supplies the tissue. Any toxic or hypoxic factor disturbs this equilibrium and provokes morphofunctional deviations in the gland. The aim of the present work is to characterise the morphofunctional changes that develop in the adrenal gland under hypoxic conditions and to assess the mechanisms by which an extract of Euphorbia lathyris may correct them.

Morphological changes of the adrenal gland under hypoxic conditions

Hypoxia, defined as an insufficiency of oxygen in the tissues, is a complex pathophysiological state that profoundly affects cellular energy exchange, metabolic processes and the secretory activity of the endocrine glands. Among the endocrine organs, the adrenal glands are particularly vulnerable to hypoxic injury because of their high metabolic activity, abundant vascularisation and elevated oxygen demand at the cellular level. Under hypoxic conditions the three cortical zones display characteristic and zone-specific morphological alterations.

In the *zona glomerulosa*, cellular vacuolation is observed, together with swelling of the mitochondria, destruction of their cristae, and an increase in the number of lipid droplets within the sarcoplasm. These features reflect early disruption of mineralocorticoid-producing cells and impairment of their energy apparatus.

In the cells of the *zona fasciculata*, the endoplasmic reticulum becomes expanded, the ribosomes lose their organised arrangement, the nuclear chromatin condenses, and the glycogen content falls sharply. This combination points to a marked decline in the biosynthetic capacity of the glucocorticoid-secreting compartment.

In the *zona reticularis*, the accumulation of lipofuscin pigment is detected, the cell nuclei progress towards a state of pyknosis, the stroma becomes densified, and apoptotic nuclear fragments appear. Together these changes indicate that the innermost cortical zone is especially prone to degenerative and apoptotic processes under prolonged oxygen deprivation.

Taken as a whole, the cortical layer responds to hypoxia with predominantly degenerative changes, while continuous oxygen deficiency suppresses the proliferative activity of the parenchyma and shifts the balance of the tissue towards apoptosis. These observations are consistent with reports that the adrenal gland is a sensitive target organ during hypoxic and toxic states and may, in the long term, contribute to endocrine insufficiency.

Euphorbia lathyris extract: phytochemical basis and corrective potential

Caper spurge (Euphorbia lathyris L.) is a member of the Euphorbiaceae family that has long been employed in traditional medicine. Phytochemical investigations have shown that the plant is rich in biologically active secondary metabolites, including

triterpenoid glycosides, diterpenoids, flavonoids, polyphenols and alkaloids, with the highest phenolic and flavonoid contents concentrated in the seed coat and root. These compounds are responsible for the well-documented antioxidant capacity of the plant, which is closely correlated with its total phenolic content and its ability to scavenge free radicals.

On the basis of this phytochemical profile, the extract exerts a complex protective action at the cellular level. Its flavonoid, triterpenoid, polyphenol and alkaloid constituents display antioxidant, detoxifying, adaptogenic and cytoprotective properties. By neutralising reactive oxygen species and stabilising cellular membranes, these compounds are well suited to counteract the oxidative and degenerative damage that hypoxia inflicts on the highly metabolically active cells of the adrenal cortex.

Mechanisms of correction

Under the influence of Euphorbia lathyris extract, several of the disturbances induced by hypoxia are reversed. The mitochondrial structure within the cells is restored and the processes of oxidative phosphorylation return towards normal, re-establishing the energy supply of the parenchyma. The level of lipid peroxidation decreases, and the hyalinosis and vacuolation observed in the stroma are reduced, while the activity of the microcirculatory system improves. These structural and biochemical recoveries indicate that the extract acts simultaneously on the energetic, oxidative and vascular components of hypoxic injury.

In the experimental groups treated with the caper spurge extract, the morphometric parameters of the endocrine cells approached normal values. At the molecular level, the expression of the proliferation marker Ki-67 increased, signalling a restoration of regenerative capacity, while the anti-apoptotic marker Bcl-2 was reactivated, indicating a shift of the tissue away from programmed cell death. This dual effect — promotion of proliferation together with suppression of apoptosis — underlies the morphofunctional normalisation of the gland.

Conclusion

1. Under hypoxic conditions the adrenal glands undergo significant morphostructural and histochemical changes, with degenerative processes predominating in the cells of the cortical layer, characterised by vacuolisation, mitochondrial swelling, condensation of nuclear chromatin and the accumulation of lipid droplets.
2. During continuous oxygen deficiency the proliferative activity of the adrenal glands decreases, while apoptotic processes intensify.
3. The extract of caper spurge (Euphorbia lathyris) exerts a complex effect on the morphological and biochemical disruptions arising under hypoxic conditions; its flavonoid, triterpenoid, polyphenol and alkaloid compounds display antioxidant, detoxifying, adaptogenic and cytoprotective properties at the cellular level.

4. Under the influence of Euphorbia lathyris extract the mitochondrial structure is restored, oxidative phosphorylation is normalised, the level of lipid peroxidation decreases, hyalinosis and vacuolisation in the stroma are reduced, and the activity of the microcirculatory system improves.
5. In the experimental groups treated with the extract, the morphometric parameters of the endocrine cells approached the norm, Ki-67 marker expression increased, and the Bcl-2 marker was reactivated.
6. On the basis of these results it is scientifically substantiated that Euphorbia lathyris extract, as a phytotherapeutic agent of natural origin, represents a promising approach for correcting the endocrine dysfunctions that arise under hypoxic conditions.

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