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The Role of Catecholamines in Maintenance of Homeostasis in Digestive Tract of Domestic Animals

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Absract Catecholamines have been identified after numerous studies at the turn of the nineteenth to the twentieth century. Their hormonal role is evident through their receptors and is very important on all of the organs and body systems. Except for the hormonal one, catecholamines also have the role of neurotransmitters. The role of catecholamines is evident in humans and domesticated animals in their digestive system. They strongly support, through their receptors, motility and secretion in stomach and small and large intestine, in a way that they relax i.e. reduce tone of smooth musculature of stomach and bowels. In that way they actively participate in normal maintenance of their homeostasis. There are evident differences in representation and distribution of adrenergic (α and β) receptors in smooth musculature of stomach as well as the small and large intestines of domestic mammals and poultry. Noradrenaline with its activity through α –adrenoceptors significantly affects the increase of secretion in gastrointestinal tract. Through β–adrenoceptors, adrenaline affects the decrease of peristaltic movements in both small and large intestine, and, at the same time, decreases tone, i.e. motility in stomach of monogastric, as well as the rumen of polygastric, animals.

Keywords: Adrenaline, digestive tract, motility, noradrenaline, receptors.

Katekolaminlerin Evcil Hayvanlarda Sindirim Sistemindeki Homeostazisin Korunmasındaki Rolü

Öz: Katekolaminler, ondokuzuncu yüzyıldan yirminci yüzyıla geçişte yapılan çeşitli çalışmalardan sonra tespit edilmiştir. Hormonal rolleri reseptörleri aracılığıyla belirgindir ve bu rol tüm organlar ve vücut sistemleri için çok önemlidir. Ayrıca, katekolaminler nörotransmitter rolüne de sahiptir. Katekolaminlerin rolü, insan ve evcil hayvanların sindirim sisteminde görülmektedir. Reseptörleri aracılığıyla mide, ince ve kalın bağırsaktaki hareketlilik ve salgılamayı mide ve bağırsakların yumuşak kas gücünü azaltıp gevşetici yönde güçlü şekilde desteklerler. Bu yolla, normal homeostazisin sürdürülmesine aktif olarak katkı sağlarlar. Mide düz kaslarının yanı sıra, evcil memeli ve kanatlıların ince ve kalın bağırsağındaki adrenerjik (α ve ß) reseptörlerinin temsil ve dağılımında belirgin farklılıklar vardır. Noradrenalin'in aktivitesi α–adrenoseptörleri aracılığıyla mide-bağırsak kanalı salgısındaki artışı önemli ölçüde etkiler. Adrenalin, β-adrenoseptörleri aracılığıyla, hem ince hem de kalın bağırsakta peristaltik hareketlerindeki azalmayı etkilediği gibi, aynı zamanda, tek mideli hayvanların midesindeki ve çok midelilerin rumenindeki gücü (hareketliliği) azaltır.

Anahtar kelimeler: Adrenalin, Motilite, Noradrenalin, Sindirim kanalı, Reseptörler.

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INTRODUCTION

In the late nineteenth and early twentieth century, a large number of scientists were engaged in researching catecholamines, or more precisely, their physiological role. That is how, in separately conducted experimental studies, Polish physiologist Napoleon Cybulski isolated and identified adrenaline in 1895, right before Jokichi Takamine, Japanese chemist, revealed the same hormone in 1900, independently of his colleague. Discovery was repeated in 1897, right in between of these two, thanks to John Jacob Abela, who found that the said substance given reduces mobility and tone of gastrointestinal system of dogs, as well as that it leads to an increase in the arterial blood pressure and called it adrenaline (1,2).

In addition to the aforementioned adrenaline - the most important biogenic amine, noradrenaline and dopamine also make up the group of catecholamines. They contain a catechol nucleus, or a benzenol ring, which contains in its position 3 and 4 two hydroxyl groups, and in position 1 a short-side chain with amino group (NH_2) in noradrenaline, and the methyl group (CH_3) in adrenaline (3). (figure 1,2).

Figure 1. Adrenaline
Şekil 1. Adrenalin

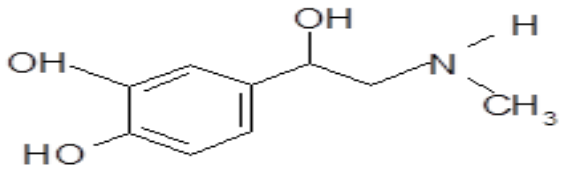
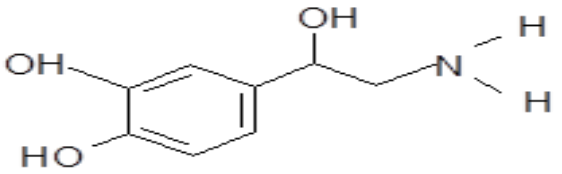


Figure 2. Noradrenaline
Şekil 2. Noradrenalin



The process of complex biosynthesis of catecholamines occurs in glandula suprarenalis. Hydroxylation of tyrosine amino acid gives dihydroxy derivative (dopa), while its decarboxylation gives noradrenaline. Adrealine is obtained by methylation of noradrenaline. By the action of the enzyme dopa decarboxylase, dopa is converted into dopamine, which in some parts of CNS (extrapyramidal system of mammals) acts as a neurotransmitter. Dopamine is under the influence of the enzyme dopamine-β-hydroxylase (DBH) and converted to noradrenaline (4,5,6). Since the dopaminergic system is not represented in digestive system, dopamine is understandably left out of work.

Noradrenaline, unlike adrenaline, has 5 to 10 times lower metabolic activity. It is a neurotransmitter and/or a hormone released from sympathetic neurons, post-ganglionic adrenergic fibres and in smaller part by the adrenal glands. Effect of the noradrenaline in the body is manifested in the form of contractions of blood vessels in the body, increased activity of the heart muscle, relaxation of smooth muscles of the stomach and intestines and spread of pupils. (7,8). Just like the adrenaline, noradrenaline activates the α - and β -adrenoceptors, where α-receptor activation is more pronounced (1,2).

During stress, due to the activation of the hypothalamus, adrenaline is released from the adrenal medulla, which are then transmitted (circulating hormones) to all of the tissues of the body by blood. About 80% of adrenaline and 20% of noradrenaline are usually excreted this way, followed by binding to and stimulation of adrenergic receptors. A positive inotropic effect on the heart, increased heart rate and its contractility, blood pressure and renal blood flow are caused. During this time, the circulation of blood in the digestive organs is reduced, motility and secretion are slowed down, and circulation in skeletal muscles and heart

is increased. Bronchi expand and the respiration rate accelerates what increases the concentration of oxygen in the blood. From the metabolic effects of adrenaline, it is important to accentuate that the liver releases increased amounts of glucose, which becomes available for conversion into energy in muscles (9,10,11) (Table-1).

Table 1. The most important effects and distribution of α- and ß-adrenergic receptors in the body (12).
Tablo 1. α- ve ß-adrenerjik reseptörlerin en önemli etkileri ve vücuttaki dağılımı (12).

Organ	Adrenergic receptor	Effect
Heart	β_1	Increased heart rate and increased strength of contraction of the heart muscle
Blood vessels - Skin and mucosae - Skeletal musculature	α_1 i α_2 $\alpha + \beta_2$	Construction Construction and dilatation
Bronchus	β_2	Relaxation
Stomach -Motility and tone	α_1 i $\alpha_2 + \beta 1$ α_1	Reduction (typically) Secretion (typically) Contraction (typically)
Bowels	α i β	Decrease in motility and tone
Uterus	β	Relaxation
Liver	β	Glycogenolysis

Furthermore, adrenaline stimulates lipolysis as well, which is accompanied by release of fatty acid and cholesterol. All these are natural effects that enable humans and animals to be in close combats or an escape from danger. This mechanism has been developed to help individuals preserve from danger (13,14).

Adrenergic Receptors

The effects of adrenaline and noradrenaline would not have been possible without the intervention of adrenergic receptors, which have been found in the CNS and in almost all peripheral tissues. By conducting a brilliant study in 1948, Ahlquist established the first pharmacological classification of adrenoceptors, and defined two types of them, which he called the α and β-adrenoceptors. Lands, and somewhat later Minneman, are responsible for a more precise establishment of sub-classifications β-adrenoceptors. They showed that β_1-adrenoceptors dominate in the small intestine and the cardiac muscle and are equally sensitive to noradrenaline and adrenaline, while the β_2 ones are responsible for relaxation of smooth muscles of the uterus, blood vessels, and respiratory organs (12,15).

These important scientific and exploratory findings were reached through pharmacological criteria, i.e. using the antagonists and agonists of these receptors. Significant differences in activity between noradrenaline and adrenaline are reflected in the following: adrenaline has a powerful effect on β-adrenoceptors and thus stronger action on the heart. It causes weak constriction of blood vessels in the musculature, while the noradrenaline's effect on them is a lot stronger (8).

Langer, in 1974, proved that the α-adrenoceptors have different pharmacological properties, and hence he divided them into subtypes: α_1 and α_2. The receptors that are located post-synaptically were annotated as α_1, and those on the peripheral sympathetic nerve endings were labelled as α_2 receptors. Performance of the radioimmunoassay analysis, as well as the conduction of a variety of other serious studies on the molecular level has deepened the knowledge of the precise classification of α_1 and α_2 receptors, as well as the classification of β-adrenoceptors into subtypes β_1, β_2, β_3. (12).

Catecholamines act, as already described, by binding to receptors in the membrane of target cells. Both groups of α and β adrenoceptors are associated with G proteins (5).

Today, it is known that catecholamines in the gastrointestinal tract act mainly through β-adrenoceptors and the effects are manifested by relaxation of smooth muscles. This way, peristalsis is slowed down. By activating α -adrenoceptors, adrenaline stimulates digestive secretion (7).

Adrenoceptors' Representation in Individual Animals

Adrenoceptors of both types are present in greater or lesser extent, on a different level, in the digestive system of humans and animals. In the smooth muscles of the rumen of small and large ruminants, in the representation and distribution of adrenergic receptors, there are opposite results, depending on whether the studies were done *in vivo* or *in vitro*. In the bodies of small ruminants, specifically in sheep, the representation of adrenergic receptors in the smooth muscle of the rumen is much higher than in the bodies of cattle, in which studies have shown that the receptors tested are present in traces. Especially, low level of representation of adrenergic receptors is found in the smooth muscles of dorsal and ventral sacs of rumen (15).

Catecholamines, by acting through the α and β-adrenoceptors, lead to a relaxation of the smooth musculature of the human colon (12). Confirmation of this previous research are also the results obtained by using certain agonists of β-adrenoceptors, where it has been proven that in the smooth muscle of the colon people (16), dogs and guinea pigs (17), rats (18), as well as in the ileum of the rats (19), β –adrenoceptors do exist. Research carried by Manara et al. (20) on the jejunum, ileum and colon of rats, and the duodenum and ileum of guinea pigs, also indicate the presence of β_3-adrenoceptors in this part of the digestive system. Similar findings were reported by Brown and Summers (21), who examined the presence of this type of receptor on the ileum of the rats, and by Hutchinson et al. (22) in the ileum of the mice. The α_1 receptors have been identified in tissues of the CNS and the PNS, especially in the hippocampus and cortex, while in the tunica muscularis of the small intestines of broilers no such receptors have been found (12). Also, the same receptor in the smooth muscle in the caecum of turkeys for fattening is not proven (8).

CONCLUSION

Based on the *in vitro* studies analysed, it can be indirectly concluded that the presence of all three subtypes of β-adrenergic receptors was determined in both layers of the tunica muscularis in stomach, as well as in small and large intestines of domestic animals, in domestic mammals as well as in poultry. Most research has been conducted on fattening broilers and turkeys. Based on the evident significant distribution of the above-mentioned receptors, it can be safely concluded that adrenaline and noradrenaline regulate motility of the digestive tract in such a way that they perform relaxation of smooth muscle, and thus slow down the peristalsis of the small and large intestine.

By application of selective agonists and antagonists in *in vitro* studies of suitable α_1 –adrenoceptors, representation of this subtype has not been determined in any of the segments of the small intestine of broilers, of the large intestine of turkeys, as well as in the rumen and the stomach of small and large ruminants, or their representation is so small that this method could not prove their existence.

Representation of the subtype α_2-adrenoceptor was found in the intestinal tract to more or less extent in all of the species, and on this basis it can be concluded that catecholamines, especially noradrenaline, which has a higher receptivity to α-adrenergic receptors than the others, affects the increase of secretions in the digestive tract.

Synthetically produced substances used in many studies that are presented in this work, which are actually non-selective and selective agonists, as well as non-selective and selective antagonists, could be considered potential medication in the regulation of disturbed functions of stomach and intestinal system of domesticated animals.

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