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# Distribution and localization of endocrine cells in the digestive system of chukar partridge (*Alectoris chukar*)

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**Abstract:** There are different types of endocrine cells that are located in the gastrointestinal system of birds and mammals. In birds, the digestive system anatomically completes the formation in the embryonic period, and in the period after hatching. Morphological and physiological differences with nutrition are formed and functionalized. The present study aimed to evaluate immunohistochemical distribution and localization of endocrine cells in the digestive tract of chukar partridges (*Alectoris chukar*) using antisera against serotonin, somatostatin, gastrin, and glucagon. In this study, after 20 chukar partridges were slaughtered, organs of the digestive system were obtained and stained for immunohistochemical analysis. In our results, various densities of glucagon, gastrin serotonin, and somatostatin positive cells in the proventriculus and small intestine were found, but only serotonin positive cells were detected in the ventriculus of chukar partridges. In conclusion, the results showed the relative frequency and distribution of some endocrine cells in the gastrointestinal tract of chukar partridge. A comparison of endocrine cell distribution in other bird species is an important topic to understand the digestive physiology for future investigation.

**Key words:** Gastrointestinal tract, endocrine cells, chukar partridge

## 1. Introduction

There are different types of endocrine cells that are located in the gastrointestinal tract (GI) of birds and mammals. Studies using immunocytochemical methods have been carried out on the gastrointestinal tract in some avian species [1–4].

In birds, the digestive system anatomically completes the formation in the embryonic period, and in the period after hatching, morphological and physiological differences with nutrition are formed and functionalized [5,6]. Enteroendocrine cells showing different numbers and density of settlements throughout the digestive tract, starting from the esophagus, are specialized digestive system cells. The histological structures and effect mechanism of these cells may vary according to the region they live in and the different living species [7]. These cells are named as argentaffin or argyrophil cells because of being able to accumulate amine precursors and exhibit amino acid decarboxylase activities, and APUD (amine-precursor uptake and decarboxylation) cells are stained with silver salts [8].

In recent years, the term "DNES (diffuse neuro endocrine system) cells" has been used [9]. There are at least 12 different types of DNES cells in the gastrointestinal tract as follows: secretin (S), cholecystokinin (CCK-pancreozymin), serotonin (enterochromaffin-EC-5HT), vasoactive intestinal peptide (VIP, D1), glicentin (enteroglucagon-GLI), neuropeptide Y (NPY), peptide YY (PYY), somatostatin (D), gastrin (G), urogastrone (gastrin inhibitory factor, GIP), ghrelin, and motilin cells, and they synthesize more than 20 hormones and neurotransmitter substances [10]. D, enterochromaffin (EC), S and G cells, known to be abundant in the mucus of the digestive system, play important roles in the regulation of gastrointestinal pH and in the secretion of digestive enzymes [11]. It is reported that these cells are in different localizations and quantities in bird species [2].

The gastrointestinal tract is covered by a single layer of epithelial cells. These cells, which are called as entereocyte, are columnar surface cells, and they have different works depending on their localization along the digestive tract [12]. The D cells release somatostatin that is able to modulate many gastrointestinal activities by paracrine and endocrine actions. The EC cells release serotonin that influences several functions including intestinal motor activity. The gastrin stimulates the parietal cells directly

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to produce acid and also indirectly via stimulation of the enterochromaffin-like (ECL) cells to release histamine. S cells produce secretin that is released upon a drop of pH value to 4 or below in the small intestine. Secretin increases bicarbonate secretion from the pancreas, liver, and duodenum. It also stimulates the secretion of bile and the release of insulin and gastric pepsin [13].

In recent years, although there are many studies about enteroendocrine cells of the gastrointestinal system [1–3,14], especially immunohistochemical works are limited to certain types of enteroendocrine cells in the avian species. The present study aims to investigate the localization and distribution of entero-endocrine cells in the digestive system of the chukar partridge by immunohistochemical methods.

## 2. Materials and methods

In total, 20 Chukar partridges were obtained from Merzifon, Amasya Patridge Hatchery and slaughtered under deep ether anesthesia. Proventriculus, ventriculus and small intestine (duodenum, jejunum, ileum) were taken from gastrointestinal system of chukar partridges and put into the 10% formaldehyde solution for 72 h at the Atatürk University Veterinary Faculty Anatomy Laboratory. All procedures were carried out in accordance with the protocol approved by the Ethical Committee (for Experimental Animal Care and Use) of the Faculty of Veterinary Sciences at Atatürk University. Afterwards, the tissues were passed through the graduated alcohol series and dehydration process and lastly the xylol series to carry out the transparency process. After this process, the tissues were embedded in paraffin blocks in appropriate positions, and sections with a thickness of 7-µm were taken.

### 2.1. Tissue sampling

Tissue sampling was carried out in the light of literature, considering the anatomical and physiological differences of the tissues [15]. Tissue sampling was performed from the inlet part of the proventriculus near the esophagus, the middle part, and the part adjacent to the ventriculus. Sampling was performed from the middle sections of the ventriculus pars dorsalis, pars ventralis and corpus, pars descendens and pars ascendens of the duodenum, Jejunum pars proximalis, and middle of the ileum. Taken serial sections were examined concerning morphological and histologic features under light microscopy after staining with Mallory's triple staining of Crossman for histological examination as described previously [16].

### 2.2. Immunohistochemical examination

The staining process was carried out by the streptavidin peroxidase method with anti-glucagon (Leica, PA0597, 1/50 dilution), anti-gastrin (Leica, NCL-GASp, 1/50 dilution), anti-serotonin (Dako, M0758, 1/50 dilution), and anti-somatostatin (Dako- A0566, 1/200 dilution), antibodies obtained by streptavidin peroxidase method using serial sections for immunohistochemical staining. Then, positive cell density was determined in the stained sections, and a score table was created. Different cells in the same region were identified, and the desired intensity was evaluated more reliably by staining these sections serially. Then, the distributions of this density, according to anatomical regions, were calculated.

### 2.3. Immunohistochemical scoring

The positive cell density of the immunohistochemical anti-glucagon, anti-gastrin, anti-serotonin, and anti-somatostatin in the stained sections were determined. For the immunohistochemical density evaluation, four parallel sections of each bird of each group were created. Also, in total, 20 different areas were investigated in each section of birds. In the final of evaluation, this density was scored as (-) absent, (+) low intense, (++) medium intense, and (+++) very intense according to previous study [17].

## 3. Results

When the distribution of glucagon positive cell density according to gastrointestinal tract sections was examined, in the proventriculus, glucagon-positive cells were found somewhere in the stomach glands, while the glucagon-positive cells in the ventriculus could not be detected. In the duodenum and jejunum, a small amount of positive cells located between the villus crypts were detected, while, in the ileum, there was a small amount of glucagon positive cells between the villus epithelium and ?. Glucagon cell density is presented in Table and Figure 1.

When the immunohistochemical anti-somatostatin positive cell densities were examined, in the proventriculus, somatostatin-secreting cells were seen among the stomach glands at medium density. In the ventriculus and jejunum sections, somatostatin-positive cells were not found. The lowest somatostatin-secreting cell density was found in ileum, while at medium density was found in the lamina propria of villus were found in the duodenum. Also, medium intense somatostatin-positive cells located in the villus lamina propria were detected in the ileum. Somatostatin cell density is presented in Table and Figure 2.

In the analysis of immunohistochemical anti-gastrin positive cell density, gastrin-positive cells stuck between the stomach glands were detected in the lamina propria of the proventriculus. While gastrin-positive cells were not found in the ventriculus, gastrin-positive cells located among the intestinal villous epitheliums were detected in intestinal sections duodenum and ileum. In Jejunum, gastrin-positive cells were found both in the intestinal villous and in the villous lamina propria. Gastrin cell density is presented in Table and Figure 3.

**Table.** Density scores of glucagon, somatostatin, gastrin, and serotonin antibodies of chukar partridge proventriculus, ventriculus, duodenum, jejunum and ileum tissues.

| Antibody | Proventriculus | Ventriculus | Duodenum | Jejunum | Ileum |
|---|---|---|---|---|---|
| **Glukagon** | + | - | + | + | + |
| **Somatostatin** | + | - | ++ | - | + |
| **Gastrin** | ++ | - | + | + | + |
| **Seratonin** | + | + | ++ | ++ | + |

Scoring expressed as (-): none, (+): few, (++): medium.

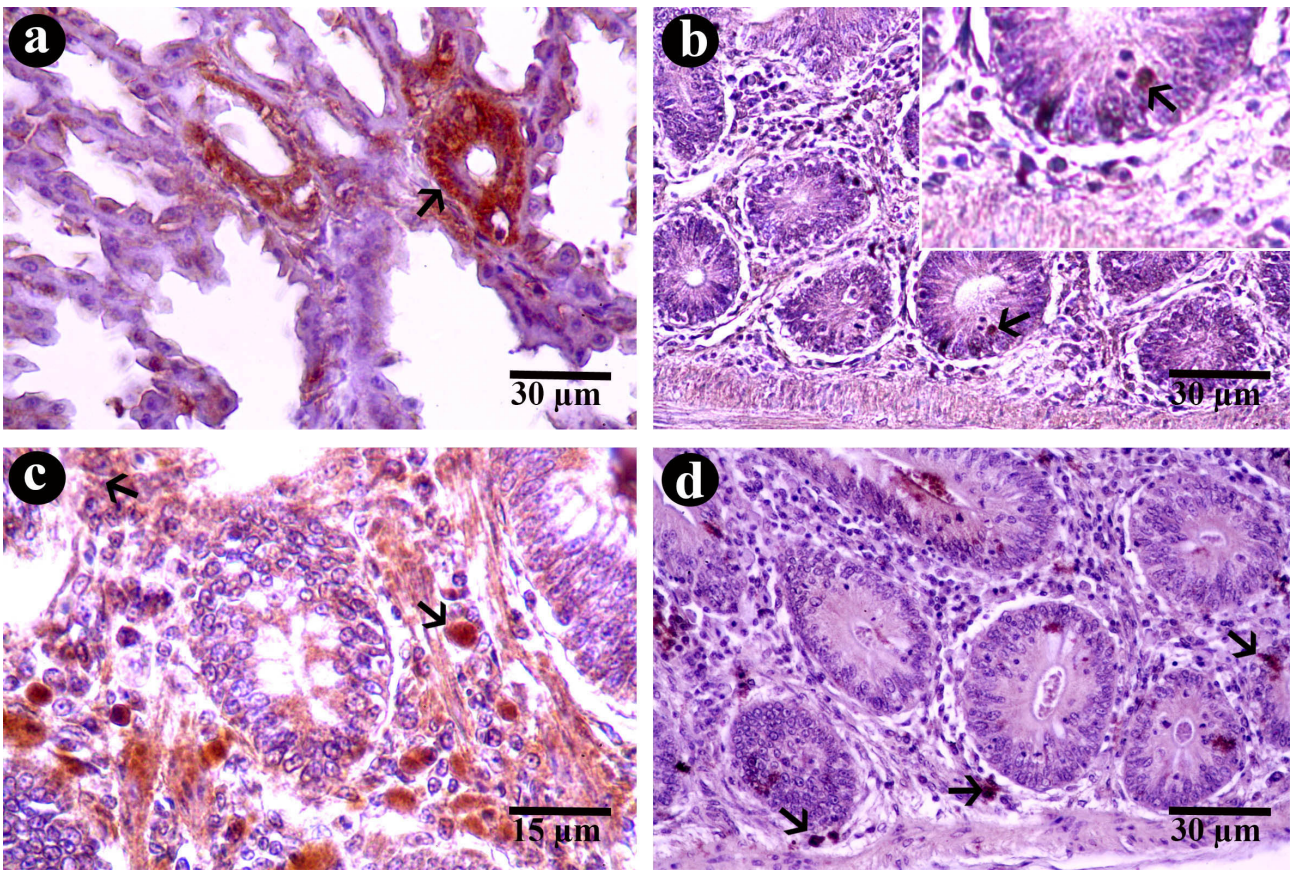


**Figure 1.** Histological image of the gastrointesitinal tract intensities of immunohistochemical anti-glucagon stained chukar partridge. (a). Proventriculus, (b). Duodenum (lower magnification), (c). Duodenum (higher magnification), (d). Jejunum, arrows: immune positive cells, immunoperoxidase staining.

In serotonin positive cell density assay, a small amount of serotonin positive cells was detected in the lamina propria layer of proventriculus and ventriculus sections. In intestinal sections of duodenum, jejunum, and ileum, medium intense serotonin positive cells were found, especially between crypt epithelium and lamina propria layer. Serotonin cell density is presented in Table and Figure 4.

## 4. Discussion

The digestive system includes organs where the foods are divided into molecular structures, and absorption is carried out in these cells. The DNES cells and the endocrine cells that produce hormonal secretion have the most important role in this absorption and regulation [18]. Many studies have been conducted on DNES cells because of the relationship between endocrine hormone

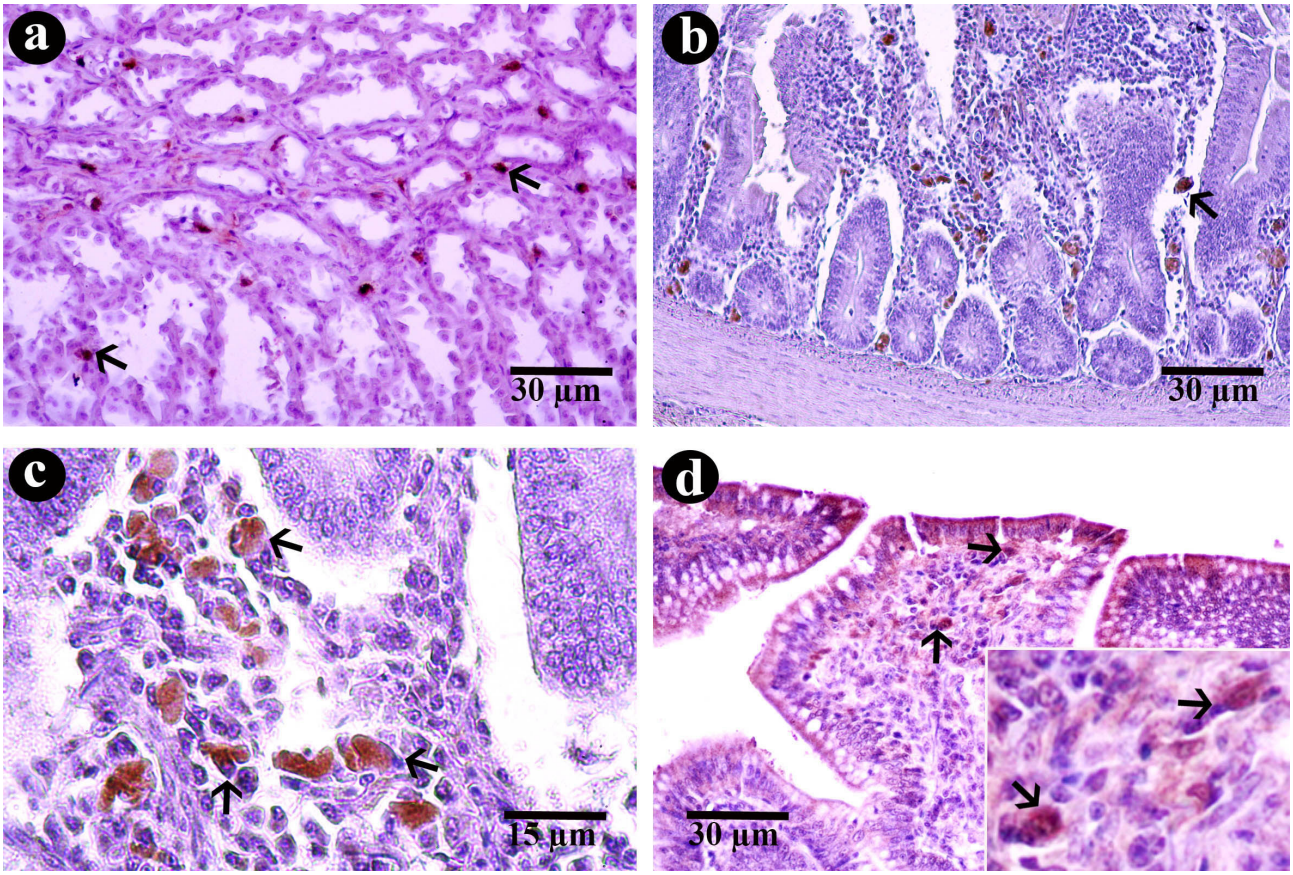


**Figure 2.** Histological image of the gastrointesitinal tract intensities of immunohistochemical anti-somatostatin stained chukar partridge. (a). Proventriculus, (b). Duodenum, (c); Jejunum, (d). İleum, arrows: immune positive cells, immunoperoxidase staining.

metabolism and live weight and egg yield of wingeds and showing different distribution according to species and organs [3,19,20].

Denomination of DNES cells among mucosal epithelium cells can be carried out either by looking at the electron microscopic features or by specific immunohistochemical staining. Endocrine cells are found as one by one or groups of clusters in the mucosa epithelium whose granules are located in the basal or apical region, and the endocrine cells can be named according to their functions (S, CCK, EC, VIP, GLI, NPY, PYY, D, ghrelin and motilin cells) [21]. These cells have been named according to their secretory products and secretory granules morphology [22]. In this study, distribution in the digestive system and histological structures of glucagon, somatostatin, gastrin, and serotonin in chukar partridge are determined.

Immunocytochemical studies have shown that glucagon-immunoreactive cells are found in the gizzard and intestines of hens [23]. Glucagon regulates the food intakes in the digestive system [24], and Glu-IR cells were found in proventriculus, duodenum, and jejunum in gray geese but not in other tissues [23]. Gulmez et al. (2003) reported that the glucagon was found entirely in the digestive tract in geese and most commonly found in the duodenum [19]. Bezuidenhout and Van Aswegen (1990) reported that glucagon IR cells are found in the proventriculus intensively in adult ostrich. However, glucagon IR cells were available in the mucosa of the lateral wall of the ventriculus in small quantities [25]. Rawdon and Andrew (1981) reported that, in addition to these, they are found in the pylorus region in small quantities in hens [26]. In this study, it was determined that as Yang et al. (2012) reported, Glu-IR cells are not found in the ventriculus in chukar partridges, unlike in gray geese, and they are found in lesser amounts in other gastrointestinal organs [23].

Somatostatin is a polypeptide-structured hormone capable of inhibiting the activities of other DNES cells and is secreted by D cells [27], which are found in the pancreas, gizzard, and intestines of mammals and winged. In the studies conducted in incubation periods of different winged species, it was reported that [28] somatostatin-positive cells were found in the proventriculus of quail [29], hen [30] and duck [29]. On the other hand, these

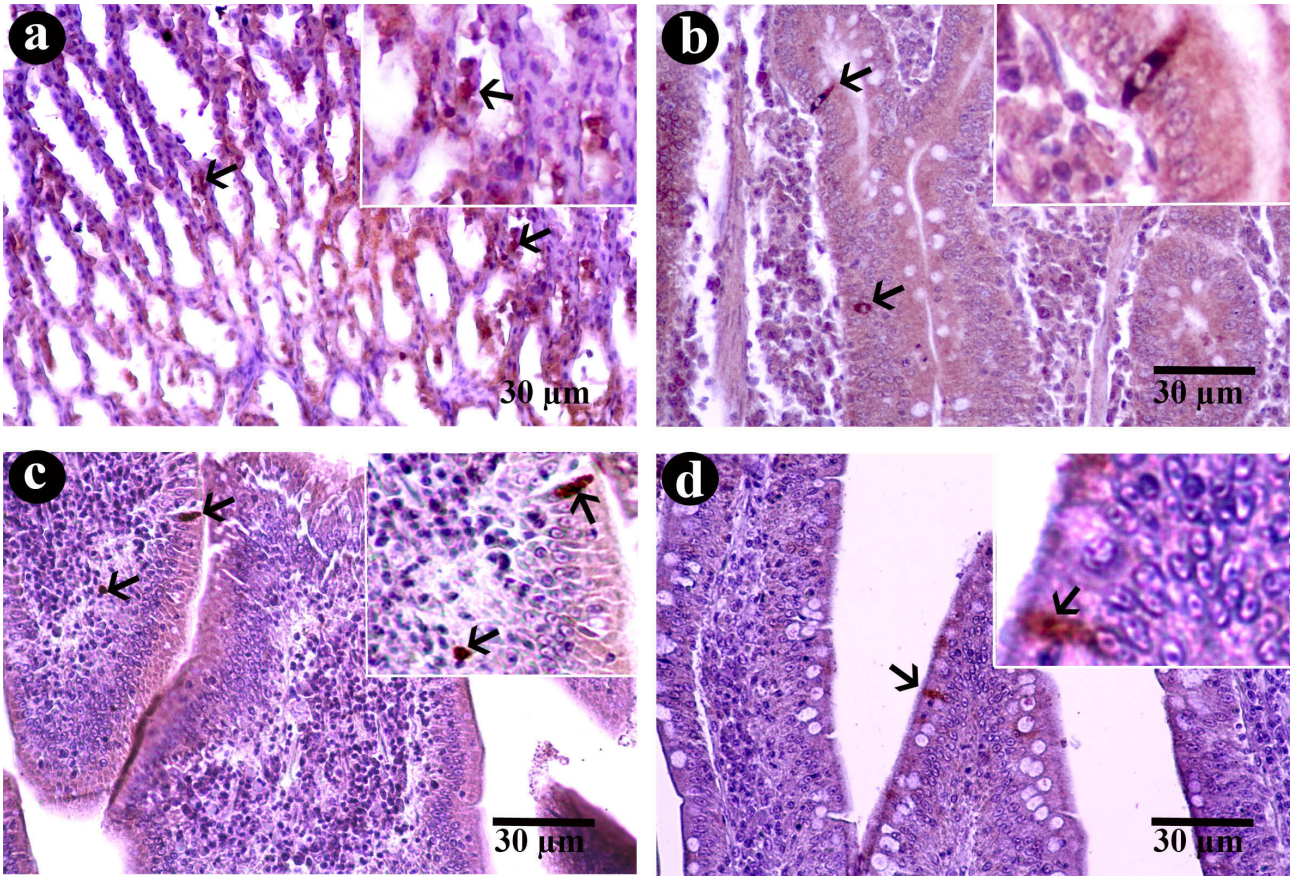


**Figure 3.** Histological image of the gastrointesitinal tract intensities of immunohistochemical anti-gastrin stained chukar partridge. (a). Proventriculus, (b). Duodenum, (c). Jejunum, (d).; İleum, arrows: immune positive cells, Immunoperoxidase staining.

cells were found in the ventriculus of hen [31], quail [32], and ducks. Bezuidenhout and Van Aswegen (1990) reported that a large number of D cells were found in the small intestines of adult ostrich [25] and chicks [33], but Gencer Tarakci et al. (2008) detected that these cells were found only in gizzard in digestive tract (a few in muscular gizzard, several in glandular gizzard) [34]. Although Çınar and Diler (2008) reported that D cells were not found in the ventriculus of adult hens [31], it was reported that they were found in the proventriculus of pigeons [35], in proventriculus and pylorus of adult hens [36] and in small intestines of geese [19] and hens [36, 37]. In addition, Aluments et al. (1977) reported that there were a large number of D cells in the proventriculus and ventriculus-duodenum gate of hens and a small number of D cells in the duodenum, although somatostatin-secreting cells were detected in the proventriculus in middle density and among the gastric glands [37]; no somatostatin positive cells were found in the ventriculus and jejunum. The lowest density of somatostatin-secreting cell was found in ileum; whereas, it was at medium density in the duodenum was found at a medium density and solitary somatostatin secreting cells located in the lamina propria of villus intestinalis of red-legged partridge.

Gastrin is a peptide-structured hormone that causes an increase in gastric acid secreted from G cells in the gizzard and duodenum mucosa [38,39]. Although G cells are generally reported to be present in gizzard and intestines in winged species, the distribution of G cells may vary in some species [2,26,40]. Gastrin immunopositive cells found in the pyloric region of ducks are present at low density in the ventriculus and duodenum [40] and different affinities of a gastrin-like peptide in the antrum of chicken [41]. In some studies [19], it has been reported that G cells were found in the esophagus and proventriculus of hens' embryos [36] or only in the proventriculus [42], in the proventriculus of hens [43,44] and quails [45], and only in the duodenum and jejunum of geese. On the other hand, there may be G cells in the middle and very low density in the Meckel diverticulum [7] and in the colon [19]. Also, in a study, it was reported that G cells were found in pylorus at high density and in duodenum in two bat species (Artibeus cinereus & Sturnira lilium) [46]. In this study, it was determined that the findings related to G

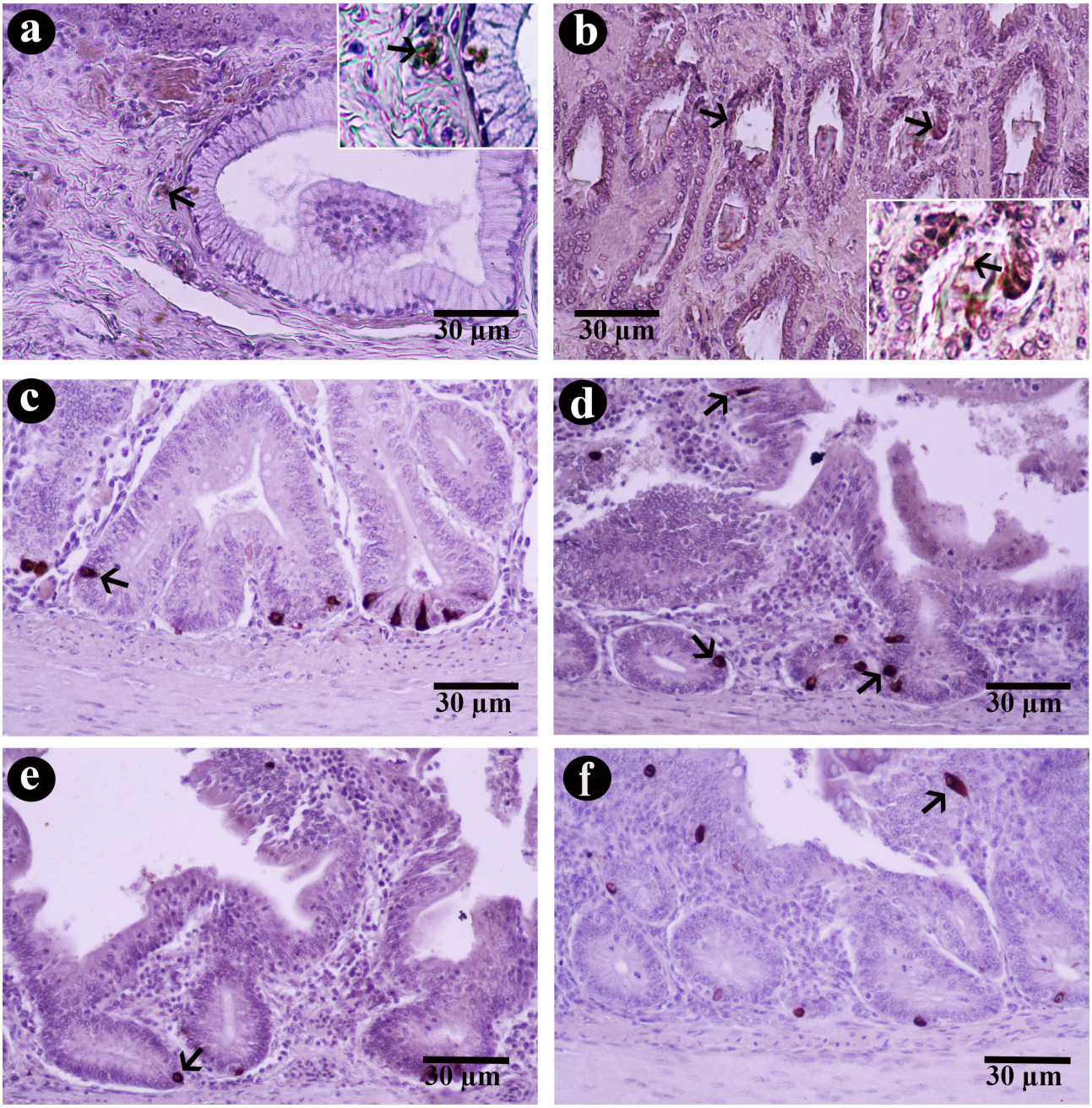


**Figure 4.** Histological image of the gastrointesitinal tract intensities of immunohistochemical anti-seratonin stained chukar partridge. (a). Proventriculus, (b). Ventriculus, (c). Duodenum, (d). Jejunum, (e). Jejunum, (f). İleum, arrows: immune positive cells, immunoperoxidase staining.

cells were consistent with with the oned obtained in some previous studies [2,36,44,45]. In addition to findings of Gulmez et al. (2003) about geese and findings of Yamanaka et al. (1989) about duodenum and jejunum in hens, it was detected that G cells were found at medium density in the proventriculus and at low density in small intestine entirely in chukar partridges.

Serotonin, which inhibits gastric acid and smooth muscle contraction, is a very effective hormone on vascular permeability. Serotonin is secreted by EC cells that are present among the surface epithelium cells and half basal of crypts in the gastrointestinal tract [47]. Although Park et al. (1999) reported that EC cells were not present in the gizzard of geese [48], Yang et al. (2012)

reported that they were present in the entire digestive system except for pylorus in gray geese [23]. Rawdon & Andrew, (1994) showed that these cells were present in the proventriculus of hens [49]. In a study of ostriches, it was reported that EC cells were observed throughout the entire digestive tract channel except for the ventriculus, but there were many EC cells in the duodenum and ileum, a few EC cells in the proventriculus and in the colon [34]. Serotonin-secreting EC cells in chukar partridges were found at medium density in the duodenum and jejunum and at low density in the proventriculus, ventriculus, and ileum.

Endcorine cells secreate autocrine/paracrine molecules, which modulate the activity of neighboring cell as well as these molecules, provide a constant control of physiological and homeostatic functions [50]. These endocrine cells of GI tract could have different distribution and localization depending on physiologic features and feeding habits of species.

In conclusion, the findings obtained in this study revealed the relative frequency and distribution of some endocrine cells in the gastrointestinal tract of chukar partridge. A comparison of endocrine cell distribution in other bird species is a significant topic for future investigation. The findings suggest that the histochemical and immunohistochemical characteristics and distribution of endocrine cells obtained in this study may be a source for future histomorphological and physiological investigations.

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