

SEA BREAM LIVER: HISTOLOGICAL AND ULTRASTRUCTURE STUDIES (I) HEPATOCYTES

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ABSTRACT

The normal structure of the liver of Gilthead sea bream, an economically valuable marine fish, was studied using LM and electron microscopy. The liver was covered by a thin fibrous connective tissue capsule, and a single layer of mesothelial cells. The parenchyma of the liver was not divided into lobules. The biliary channels and vascular elements seemed to be randomly dispersed throughout the parenchyma.

The liver was formed of a mass of cells penetrated by sinusoids. Within the parenchyma, the hepatocytes spread out as irregular cords arranged in two cellular layers surrounded by sinusoids. Hepatic sinusoids were lined by endothelial cells with elongated dark nuclei. The endothelium separates the space of Disse incompletely from the lumen of sinusoids. The hepatocytes were hexagonal in shape, had spherical pale- stained and centrally located nuclei that showed one or more nucleoli. Binucleated cells were sometimes visible. ultrastructurally hepatocytes showed large, spherical and rounded nuclei. The nucleus contained one or more prominent nucleoli. It was pale euchromatic and showed some heterochromatin at the periphery. The microvillus surface of the hepatic cells was clear in the space of Disse, interhepatocytic surface and canalicular surface facing the bile canaliculi. The cytoplasm had abundant amounts of R.E.R while S.E.R. was few. Numerous mitochondria, large amount of glycogen as well as many lipid droplets were also seen.

Different cells rather than hepatocytes were observed in the parenchyma. Melanomacrophage centers appeared as group of macrophage with chromolipoid material and melanin pigments. A second type of non hepatocytic cell was located in the perisinusoidal space and called "perisinusoidal cell". A third non hepatocytic cell type was found wedged in between adjacent hepatocytes at the sinusoidal side. Between hepatocytes in a midst position there was another type of cells with elongated nuclei and dispersed chromatin, with cytoplasmic processes extending between hepatocytes. The intraparenchymal macrophage cells were located among the hepatocytes.

INTRODUCTION

Fish have some unique anatomical and physical characteristics that are different from mammals; however, they still possess the same organ systems that are present in other animals. Organ systems of fish vary to some extent from that of mammals due to the aquatic environment they live in. Gilthead sea bream (*Sparus aurata*) is a species of great economical importance for the Mediterranean mariculture industry. Rapid growth rates, good productivity per unit volume of water and economic food conversion makes sea bream a suitable fish for the needs of modern aquaculture. This group of fish has long been extensively bred in lagoons in Egypt, France, Greece, Tunisia, Turkey, Spain and in Italy. But since the 1970s (when artificial reproduction techniques were established), growing these fish has become more intensive in ponds, tanks, raceways and cages. Nowadays there are only a few land-based farms while the major part of the on growing takes place in sea cages (*Stephanis, 1996*).

Marked attentions are focused on liver of fish. This can be attributed to the fact that, the liver plays a major role in the process of vitellogenesis of oocytes (production of yolk protein) and in the energy production during spawning (*Wallace, 1978; Quebral, 1991; Toru & Shozo, 1998 and Arukwe & Goksoyer, 2003*). With the escalating threat of pollution, the search for histological indicators of environmental quality and physiological stress achieves increasing importance. The liver is an integrator in physiological and biochemical functions and thus alterations, for example in its structure, might be expected under certain toxic circumstances (*Hinton & Laurèn, 1990 and Rocha, Monteiro and Pereira, 1994*). Besides it is used as biomarker for determining environmental quality (*Ashley, 1972; Malins & Haimanot, 1991 and González, Crespo and Bruslè, 1993*).

As a preliminary test for the evaluation of pathological reactions, it is necessary to establish the normal structure of the liver; so that, morphological changes associated with age, sex, season or nutritional stage, may be confused with toxic induced lesions. Additionally, because no solid basic studies are carried out, the nomenclature used for the liver of mammals is frequently applied to fish liver, generating misinterpretations in several occasions (*Hampton, McCuskey, McCuskey & Hinton, 1985*). From the above, and because of the advantages of these fish as a food source, sea bream deserve some attention. This work concerned the normal histological and cytological organization of the liver in sea bream fish species in addition to the histochemical remarks involving its biochemical functions. In order to clarify the precise organization of liver in these important species.

MATERIAL AND METHODS

The material used in this study was Gilthead sea bream obtained from some private fisheries near the Mediterranean sea in EL-Manzala lagoon. Forty adult hermaphrodite fish ranged between 250-400 gm in weight were collected over the period from September 2003 to April 2004.

The samples for light microscopic investigation were dissected finely from the fish. Pieces of about 1 cubic cm. were taken quickly from liver, then transferred to 10% neutral buffered formalin, Bouins fluid, Sussa fixative, Zenker formol and Gender's fixative. The tissue blocks were processed and embedded in paraffin wax. Tissue sections of 5-6 μm thicknesses were prepared and stained with Harris haematoxylin and eosin(H&E), Crossmon's trichrome stain, Gomori's reticulin, PAS and Best's carmine methods. The fixatives and staining methods were used as outlined by **Crossmon (1937); Cook (1974); Drury & Wallington (1980) and Bancroft & Stevens (1982).**

For the ultrastructural purposes, small pieces of about 1mm³ of the liver were immediately fixed in a mixture of paraformaldehyde/ glutaraldehyde buffered with 0.1 M phosphate buffer PH 7.2 conc. 2.5% (**Karnovsky, 1965**). Specimens were post fixed in 2.0% buffered osmium tetroxide and finally embedded in Spurr. Semi-thin sections of 1 μm thickness were obtained and stained by toluidine blue and examined with the light microscope. Thin sections were obtained and were double stained using uranyl acetate and lead citrate then examined by electron microscope.

RESULTS

The liver of Sea bream was covered by a thin fibrous connective tissue capsule, and a single layer of mesothelial cells (**Fig.1**). The capsule was formed mainly of collagen fibers (**Fig.2**). The parenchyma of the liver was not divided into lobules. The biliary channels and vascular elements seemed to be randomly dispersed throughout the parenchyma and it was formed of hepatocytes which were organized into plates separated by dilated sinusoids (**Fig. 3**). In some specimens the hepatic parenchyma appeared to be formed of large vacuolated hepatocytes that were radially arranged around tiny hepatic sinusoids in the form of liver cords (**Fig.4**). A framework of reticular fibers outlining the sinusoids, marking the tubular arrangement of hepatocytes, and around the wall of blood vessels as well as, the acini of exocrine pancreas (**Fig.5**).

The venous elements varied from small to large venules. Some large veins were completely isolated from any other type of element, either an arterial vessel or a biliary duct. Other large veins (portal vein) and its branches were appeared associated with exocrine pancreatic tissue (**Fig.6**). The sinusoids ran from the portal veins in irregular and tortuous manner at the periphery of the liver and joined more centrally to form the hepatic vein centrally (**Fig.7**). At this level the portal vein was easily differentiated from the hepatic vein where its lumen was engorged with blood and its wall was surrounded by collagen fibers, reticular fibers, the exocrine part of the pancreas and occasionally a melanomacrophage (**Figs 5 & 6 & 8**).

A network of sinusoids surrounded, partially or completely, the hepatic parenchymal cells. The sinusoids appeared wide, irregular and tortuous. Sections stained with toluidine blue showed wide hepatic

sinusoids that were lined by endothelial cells with elongated dark nuclei. **(Fig.9)**.The endothelium separates the space of Disse completely from the lumen of sinusoids. The body of these cells was the thickest part, which contained an elongated nucleus with peripheral chromatin and a thin perikaryonal cytoplasm **(Fig.10)**.

The liver was formed of a mass of cells penetrated by sinusoids. Within the parenchyma, the hepatocytes spread out as irregular cords arranged in two cellular layers surrounded by sinusoids . The hepatocytes were hexagonal in shape, had spherical pale- stained and centrally located nuclei that showed one or more nucleoli. Binucleated cells were sometimes visible. The cytoplasm was varied from slightly acidophilic to highly vacuolated depending on the season of sample taking **(Figs.3&4&7)**.

Ultrastructurally hepatocytes showed large, spherical and rounded nuclei. The nucleus contained one or more prominent nucleoli. It was pale euchromatic and showed some heterochromatin at the periphery. The microvillus surface of the hepatic cells was clear in the space of Disse and canalicular surface facing the bile canaliculi. The microvilli of the intercellular bile canaliculi obscured its lumen **(Fig.11)**. The cytoplasm had abundant amounts of well developed rough endoplasmic reticulum (R.E.R.) in parallel arrays around the nucleus near the cell membrane. Numerous oval to elongated mitochondria with long interdigitated cristae were evenly distributed throughout the cytoplasm. They have a granular matrix of variable electron density. Different sizes of vacuoles, usually found associated with the mitochondria and also detected under microvilli **(Figs.12 & 13)**. Large amount of glycogen granules were concentrated at the peripheral sides of the cells facing

blood sinusoids (**fig. 14**). A large lipid droplet was seen in the cytoplasm close to glycogen aggregations. Profiles of smooth endoplasmic reticulum (SER) were fewer than those of RER. Lipid droplets sometimes occupied a substantial proportion of the cytoplasm. The intercellular space was relatively narrow and the cell membrane of the adjacent cells showed desmosomal junctions. Electron-dense bodies were located mostly in a juxtannuclear position; they corresponded to peroxisomes or lysosomes (**Figs. 11&13 &15**).

Serial sections demonstrated that the parenchyma of liver contained an association between bile duct lined by cuboidal cells with acidophilic cytoplasm and an arteriole. This association was enclosed by connective tissue fibers (**Fig. 16**). The sizes of this type of association were very variable.

Different cells rather than hepatocytes were observed in the parenchyma. Melanomacrophage centers appeared as group of macrophage with colored material and melanin pigments. They were found associated with large blood vessel and randomly scattered in the hepatic parenchyma either as isolated melanomacrophage cells or form well structured centers. Histochemically, a melanomacrophage center reacted positively with PAS (**Figs.17**).

The hepatic sinusoids appeared lined by endothelial cells and separated from the hepatocytes by space of Disse. The space of Disse contained abundant slender microvilli projecting from parenchymal cells where a second type of non hepatocytic cell was located and may be called "perisinusoidal cell" (**Fig.18**). Perisinusoidal cells were located immediately underneath the endothelial lining, and had elongated,

angular nuclei, rich in heterochromatin. Sometimes the perikaryon was found in recesses between hepatocytes, in which case the nuclei tend to be less elongate but with deep indentation. There were two types of perisinusoidal cells; some cells have one or few cytoplasmic paranuclear lipid droplets (**Fig.19**). Other Type of perisinusoidal cells were observed in the space of Disse, which appeared devoid of lipid droplets, with angular nuclei having abundant heterochromatin; and surrounded by microvilli (**Fig.20**). A third non hepatocytic cell type was found wedged in between adjacent hepatocytes at the sinusoidal side (**Fig. 21**). These cells had large irregular nucleus with abundant heterochromatin, nuclei occupying most of cell volume (**Fig.22**). The cytoplasm appeared few without apparent organelles. Between hepatocytes in a midst position there was another type of cells with elongated nuclei and dispersed chromatin, with cytoplasmic processes extending between hepatocytes (**Fig.23**). The intraparenchymal macrophage cells were located among the hepatocytes. They had large lobulated nuclei with marginated heterochromatin. The cytoplasm was pale, and showed a few short extensions (**Fig.24**).

DISCUSSION

Histologically, the liver was covered by thin fibrous connective tissue capsule which was invested by a single layer of mesothelial cells. This was agreed with the results recorded by *Chapman (1981)* in rainbow trout, and *El-Habbak (1995)* in Tilapia. The latter author added that numerous large number of pinocytotic vesicles, a well developed Golgi apparatus and a cell membrane which showed high activity for both endocytosis and exocytosis. The same author speculated that the covering epithelium plays a role in transferring some hepatic products to the peritoneal cavity.

The connective tissue stroma was represented mainly by collagen and reticular fibers surrounded both the hepatic and portal veins. The stromal elements were found around the branches of bile ducts and supporting the exocrine pancreas. Connective tissue stroma was also concentrated in the subcapsular and was restricted to collagen fiber in the space of Disse. A similar stroma was seen in the liver of largemouth bass fingerlings (*Hinton, Snipes and Kendall, 1972*), in the adult liver of catfish (*Hinton & Pool, 1976*) and other teleosts (*Howse, Overstreet, Hawkins and Franks, 1992*).

The hepatic parenchyma of sea bream was formed of a mass of cells penetrated by sinusoids. Within the parenchyma, the hepatocytes spread out as irregular cords arranged in two cellular layers surrounded by sinusoids. The hepatocytes in some instances were organized radially in tubules. The tubular arrangement of the hepatocytes in sea bream resembles that recognized in other studies as in the Atlantic croaker, (*Eurell & Hanesly, 1982*) and Grey mullets (*Biagianti- Risbourg, 1991*), the former author showed that hepatocytes were arranged as tubules of hepatocytes that surrounded a sinusoid.

The blood sinusoids of sea bream liver appeared wide, irregular and tortuous lined by endothelial cells with elongated dark nuclei. The structure of the sinusoidal endothelial cells in sea bream agreed with what had been seen in other fishes. The endothelium was discontinuous with fenestrae lacking diaphragms, and rest on no basal lamina and there were desmosomal junctions between the cytoplasmic processes. The same appearance was described in catfish (*Hinton & Pool, 1976*), goldfish (*Nopanitaya, Carson, Grisham and Aghajanian, 1979*), flatfish

(*Tanuma, Ohato, & Ito, 1982*), and other teleosts (*Ferri & Sesso, 1981a*). *Tanuma & Ito (1980)* added that the desmosomal junctions between the endothelial cells apparently reinforce their connection and make up a strong framework supporting the hepatic tissue. The similarity of structure means that this may be the case in sea bream as well.

In this study the venous elements were represented by large veins which were completely isolated from any other type of element, either an arterial vessel or a biliary duct. Other large veins (portal vein) and its branches appeared associated with the exocrine pancreatic tissue. The veins without any associated pancreatic tissue were probably central veins, a finding stated by several authors (*Hinton et al., 1972, Eurell & Haensly, 1982 and Robertson & Bradely, 1992*). The present investigation clarified the absence of hepatic triads. This result disagreed with *Eurell & Haensly (1982)* in the Atlantic croaker, *Leatherland & Sonstegard (1988)* in coho salmon, *Robertson & Bradely (1992)* in Atlantic salmon and *Abd El-Mohdy (1993)* in fresh and salt water fishes. The previously mentioned authors described a portal triad in their studied fishes resembles that of mammals.

The hepatocytes were hexagonal in shape, had spherical pale-stained and centrally located nuclei that showed one or more nucleoli. The cytoplasm varied from slightly acidophilic to highly vacuolated. This arrangement was detected in trout (*Anderson & Mitchum, 1974*) and in Tilapia (*El-Habback, 1995 and Abd El-Fatah, 1999*). The above results were contradicting with *Hampton, Lantz, Goldblatt, Lauren and Hinton (1988)* in trout, *Abd El-Mohdy (1993)* in catfish and *Speilberg, Evensen and Nafstad (1994)* in atlantic salmon. Light cells and dark

cells were detected in trout and salmon hepatic parenchyma (*Hampton et al., 1985 and Leatherland & Sonstegard, 1988*). There are two general views of hepatocytes, one appeared highly vacuolated and, on the contrary, the other was not vacuolated but very basophilic. These aspects were mainly imputed to a greater or lesser amount of glycogen, lipids, or rough endoplasmic reticulum. The hepatocytes were smaller in Atlantic croaker than in other fish species (*Eurel & Haensly, 1982*). *Bucke & Feist (1993)* proved that not only vacuolization resulting from glycogen and lipid deposits, but also that the affinity to haematoxylin correlates with a depletion of these components. We might conclude that the different appearance of hepatocytes of sea bream was related to season of sampling and nutritional status. The cell surface of the sea bream hepatocytes reveals three cited surface possibilities, it showed the surface forming a bile canaliculus, originally described by *Chapman (1981)*, the surface facing an adjacent hepatocytes and the surface facing the subendothelial space i.e. space of Disse. This result came in accordance with that stated by *El-Habbak (1995)* who added additional possibility for another surface facing the serosa.

Rough endoplasmic reticulum in the hepatocytes was cited in all fish species under cytological investigations. However, it was present with abundant cisternae and parallel form distributed allover the most of cytoplasm and associated with free ribosomes (*Weis, 1972, and Takahashi, Sugawara & Sato, 1977*) in salmon; this came in agreement with our finding. However, little amount of cisternae were observed in hepatocytes of zebra fish (*Miscalencu, Iordachel, Mailat, Mihaescu and Untu, 1978 and Peute, Van der Gaag & Lambert, 1978*). Hepatocytes in

carp and spart contained moderate amount of cisternae (**Kramar, Goldenberg, Bock & Klobucar, 1974 and Quaglia, 1976**). Mitochondria in the sea bream resemble those found in other teleosts (**Byczkowska-Smyk, 1967, Welsch & Storch, 1973, Hinton & Pool, 1976, Chapman, 1981, El-Habback, 1995 and Konsowa & Abd El-Gawad, 2001**) and located in the basal cytoplasm near the space of Disse. This concentration of mitochondria might be because of the activities occurring at this surface of hepatocytes. Smooth endoplasmic reticulum was found in small amount mainly as vesicle. Similar results have been reported in other teleosts (**Byczkowska-Smyk, 1967, Welsch & Storch, 1973, Yamamoto & Egami, 1974 and El-Habback, 1995**). However there were also quantitative variations since **Byczkowska-Smyk (1971)** who described a voluminous smooth endoplasmic reticulum in *Leuciscus cephalus* and *Rutilus rutilus* fish species. Considering the fact that this organelle was involved in bile salt formation and in glucuronoide conjugation of bilirubin (**Jones & Spring-Milis, 1988**).

Hepatocytes of sea bream were characterized by a range of organelles, including abundant rough endoplasmic reticulum and often a Golgi complex, indicating protein synthetic capability. Large glycogen deposits were also common in hepatocytes. The extensive glycogen stores in hepatocytes of commercially reared sea bream could be related to the carbohydrate content of many commercial diets (**Scarpelli, Greider & Frajola, 1963 and Leatherland, 1982**). The liver parenchymal cell of sea bream contains limited quantities of lipid stores. The same results were reported in Atlantic salmon (**Robertson & Bradley, 1992**). This may relate to their hepatic lipid storage capacity or

rate of lipid utilization. Alternatively, nutritional factors might influence hepatic lipid stores. While, in salmon the lipid appeared in the form of varying sized droplets (*Leatherland & Sonstegard, 1988*). In carp, *Byczkowska- Smyk, (1967)* and *Eastman & DeVries (1981)* found lipid in large quantities or even large masses in the cytoplasm.

In agreement with *Agius (1980)*, melano-macrophage centers were generally consisted of an accumulation of closely packed highly pigmented, phagocytic cells. They were dispersed in the liver as a group of macrophage with chromolipoid material and melanin pigments. It had been suggested that melano-macrophage centers might be a special type of granuloma formed by the accumulation of circulating mononuclear phagocytes that had ingested foreign materials (*Vogelbein, Fournie, and Overstreet, 1987*). Perisinusoidal cells were located immediately underneath the endothelial lining, there were two types of perisinusoidal cells; some cells had one or few cytoplasmic paranuclear lipid droplets. Only non membrane bounded lipid droplets were observed. In the contrary, two type of lipid droplet present in the perisinusoidal cell of adult lamprey (*Wake, Motomatsu & Senoo, 1987*). These cells were suggested to store retinol in lamprey liver. Other Type of perisinusoidal cells were observed in the sea bream liver, which appeared devoid of lipid droplets, and seen in a number of other teleosts (*Nopanitaya et al., 1979*). These cells were identified as empty fat storing cells (*Tanuma & Ito, 1980 and Fujita, Tamura and Miyagawa 1980*). We suggest that the empty perisinusoidal cell might be modified fibroblast. These cells together, with other interstitial cells detected in the liver parenchyma of sea bream might provid a supportive framework to the hepatic parenchyma and compensate for the lack of connective tissue stroma in sea bream liver.

Kupffer cells have been identified in trout (*Anderson & Mitchum, 1974*), channel catfish (*Hinton & Pool, 1976*), goldfish (*Fujita et al., 1980*), brown bullhead (*Hampton et al., 1987*) and other teleosts (*Ferri & Sesso, 1981b and Hinton, et al., 1984*). However, ultrastructural examination of normal liver in at least 50 other teleost species suggested that Kupffer cells were rare or absent (*Kendall & Hawkins, 1975, Hacking, Budd and Hodson, 1977, Langer, 1979, Nopanitaya et al., 1979, Chapman, 1981, Tanuma et al., 1982 and Sato & Yamamoto, 1983*). In sea bream we report a cell located wedged in between adjacent hepatocytes at the sinusoidal side. These cells were similar in appearance to those described by *Anderson & Mitchum (1974), Hinton & Pool (1976), Hinton, Walker, Pinkstaff and Zuchelkowski (1984), and Hampton, Klauming & Goldblatt (1987)*. The intraparenchymal macrophage was located among the hepatocytes. These cells have large lobulated nuclei. The same structure was reported in many fishes, including rainbow trout (*Hampton et al., 1988 and Hampton, Lantz and Hinton, 1989*) and Atlantic salmon (*Robertson & Bradley 1992*).

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Fig. (19): Electron micrograph showing perisinusoidal cell (p) containing vacuole (v). Notice hepatocyte (h) contain glycogen (g); lipid (l) droplet and its micro-villus projection (m) to the sinusoid (s). (Uranyl acetate-Lead citrate X10000).

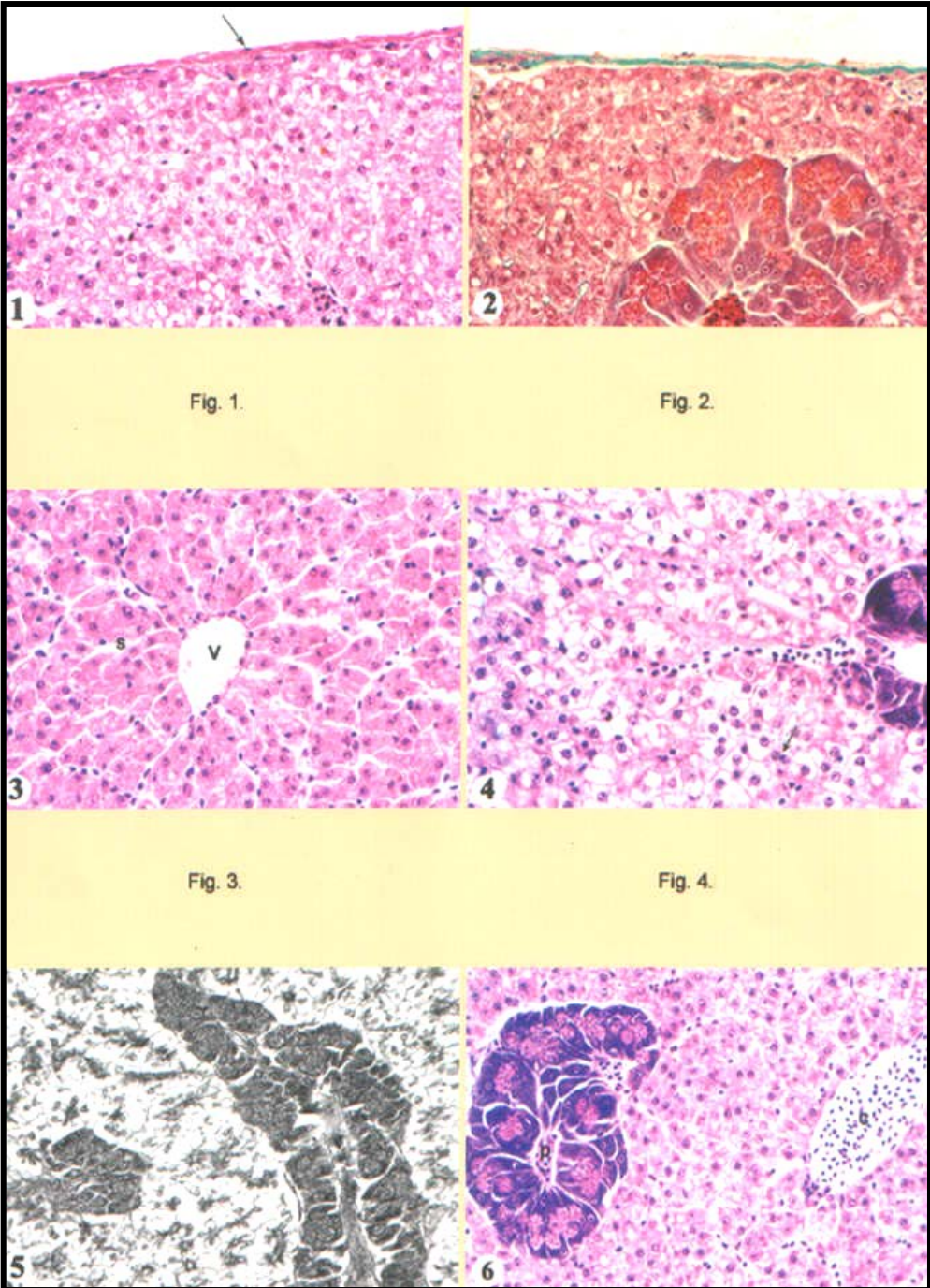
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Fig. (24): Electron micrograph of sea bream liver showing intraparenchymal macrophage between hepatocytes without any means of junctions. (Uranyl acetate - lead citrate X15000).



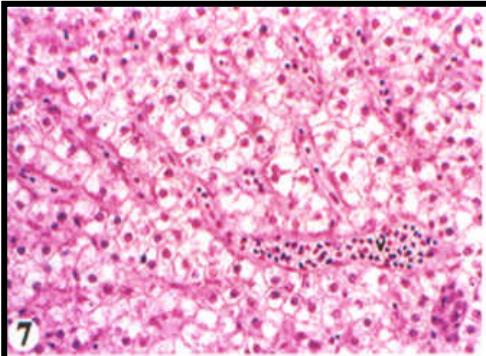


Fig.7

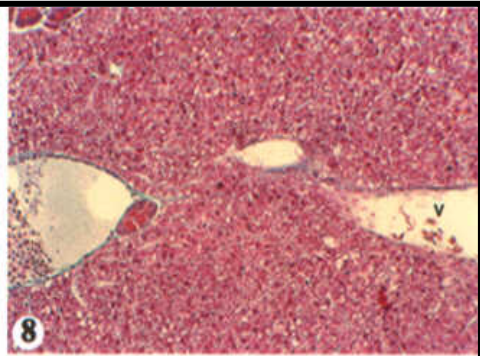


Fig.8

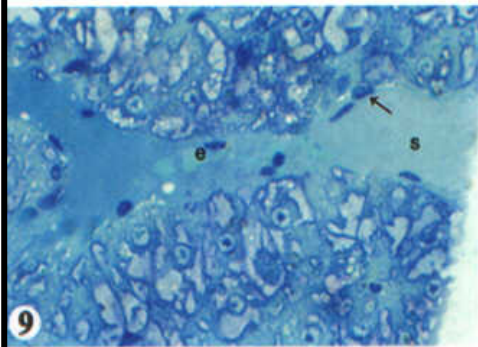


Fig.9

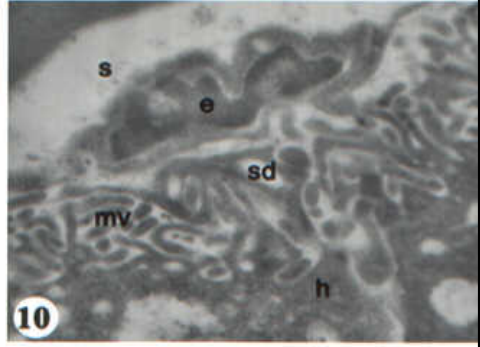


Fig.10

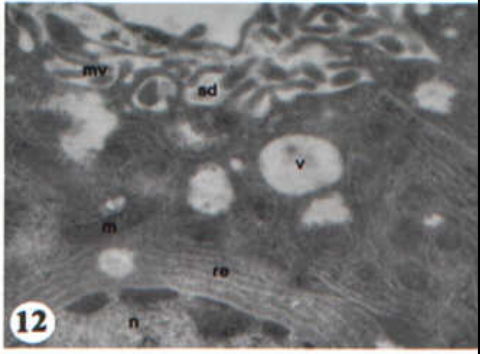
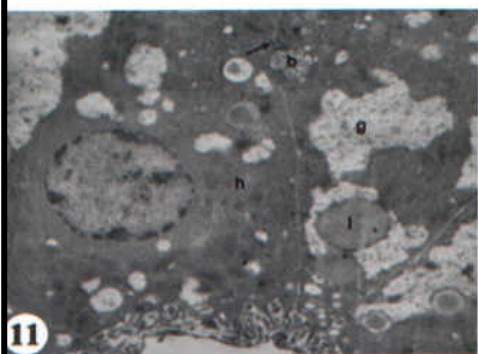




Fig. 13

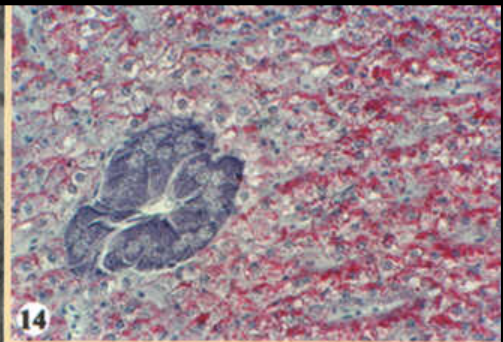


Fig. 14

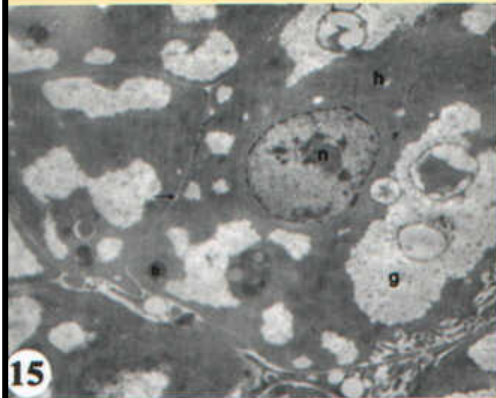


Fig. 15

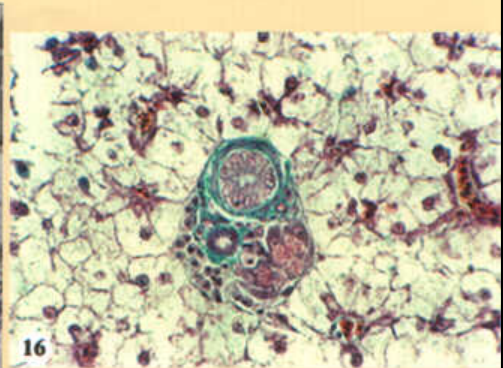
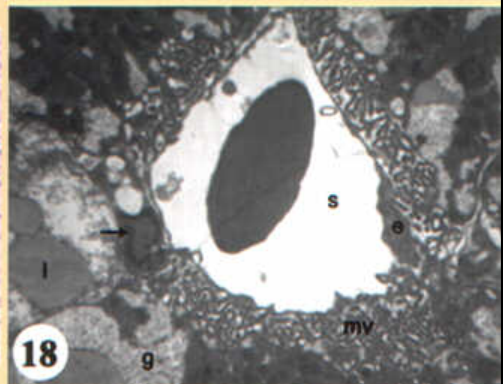
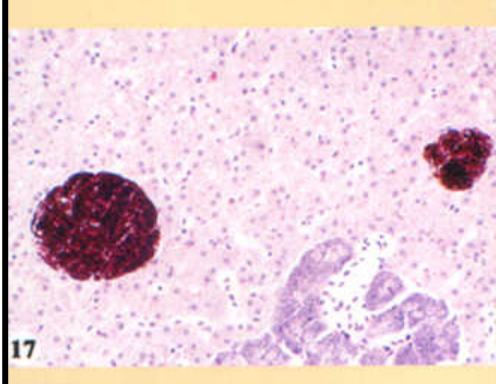


Fig. 16



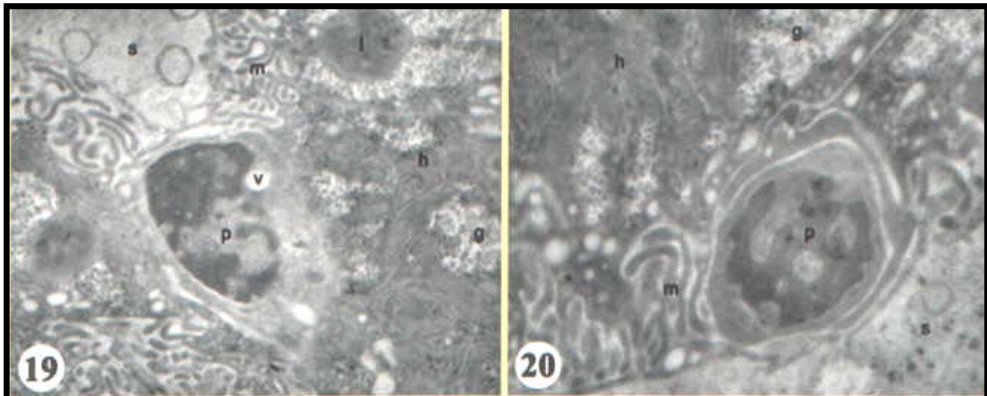


Fig. 19

Fig. 20

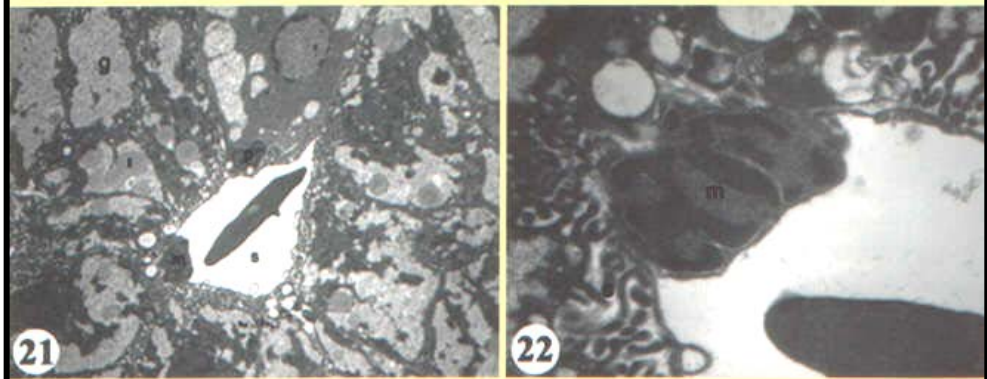
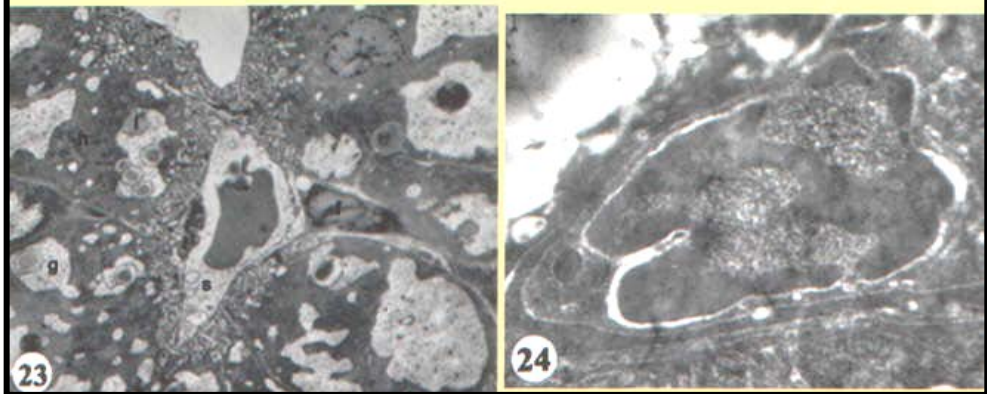


Fig. 21

Fig. 22



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كبد سمك الدنيس: دراسات بالمجهر الضوئى والالكترونى (I) الخلايا الكبدية
 خ./ طتهجك ضئظ - خ./ فئذئك خئئعو - خ./ جئئك كئكحو - خ./ لئئت بعئ ذئ.
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وجد أن كبد سمك الدنيس مغطى بمحفظة رقيقة من النسيج الضام الليفى و التى يغطيها صف واحد من الخلايا الحرشفية. لوحظ ان نسيج الكبد لا يتواجد فى صورة فصوص وان المسارات المرارية و العناصر الوعائية تنتشر بشكل عشوائى فى نسيج الكبد. يتألف الكبد من كتلة من الخلايا تخترقها جيبيات دموية و أن الحبال الخلوية غير منتظمة و شملها خليتان. تحاط الجيبيات الدموية بشبكة من الألياف الشبكية و كذلك حول الأنابيب الخلوية الكبدية و فى جدر الاوعية الدموية و ايضاً حول وحدات البنكرياس. تختلف العناصر الوريدية من الوريدات الصغيرة الى الكبيرة , أما الاوردة الكبيرة فتت عزل عن باقى العناصر و التى هى وعاء شريانى أو قناة مرارية اما باقى الاوردة الكبيرة و التى تتمثل فى الوريد البابى و فروعة فى تظهر مرتبطة بالنسيج البنكرياسى خارجى الافراز. الخلايا الكبدية تأخذ شكلاً سداسياً وحتوى على أنوية كروية باهتة الصبغة و التى بها نوية أو أكثر. قد نرى بعض الخلايا الكبدية ثنائية النواة. تتراوح بلازما الخلية من الحمضية إلى الفجوية اعتماداً على الفصل الذى أخذت فيه العينة. النواة الكبدية تحتوى على كروماتين منتشر وبعض الكروماتين المكس, أما السطح المزود بخميلات فيواعة مساحة ديس, والخلايا المجاورة والقنوات بين الخلايا. تحتوى بلازما الخلية على تجمعات كثيرة من الشبكة الهيولية الخشنة. الميتوكوندريا متطاولة وكثيرة أو بيضوية ومنتشرة فى البلازما الخلوية. تحتوى الخلايا أيضاً على فجوات بجوار الميتوكوندريا وكميات كبيرة من حبيبات الجليكوجين و التى تتركز فى أطراف الخلية. تقل نسبة الشبكة الملساء كما تتواجد أجسام كثيفة الكترونياً فوق النواة. يتواجد خلايا أخرى فى نسيج الكبد , مثل مراكز الخلايا البلعمية - الخلايا الصبغية , وهى تتواجد كمجموعة من الخلايا البلعمية مع صبغه الميلانين. النوع الاخر من الخلايا غير الكبدية يتوضع فى المسافة حول الجيبيات وتسمى هذه الخلايا "خلايا جوار الجيبيات". بين الخلايا الكبدية أيضاً تتواجد خلايا أخرى ذات ذوائد بلازمية تنتشر بين الخلايا الكبدية. الخلايا البلعمية داخل الكبد تتوضع بين الخلايا الكبدية. تحتوى هذه الخلايا على أنوية مفصصة و بلازما باهتة , وميتوكوندريا , وعدد قليل من الشبكة البلازما الخشنة و اجسام متبقية مبلعمة.