COMPARISON OF PORK LIVER IN MICROSCOPIC ANATOMY: HEPATIC VASCULATURE AND ZONATION

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ABSTRACT

Liver is a kind of nutrient-dense superfood which is rich in protein, low in calories and packed with essential vitamins and minerals. Pork liver is cheap and also readily available from grocery stores and butchers. In Thailand, there are various sources of pork liver according to feeding and taking care. Regarding the different treating, liver is the most vital organ which plays the dominant role in digestion processing, drugs and toxins filtering and clearing, in which the characteristics of liver represent the health status. Thus, this study aimed to investigate the microscopic anatomy of various sources of pork liver focused on the hepatic vasculature and hepatic zonation. Three various sources of pork livers were bought from three different grocery stores: natural pork liver, Beta-agonist free pork liver, and hygienic pork liver. Pork livers were cut and fixed in 10% neutral buffered formalin. Fixed sample tissues were then histological processed, paraffin embedded, tissue sectioned and Hematoxylin and Eosin stained. Pork liver slides were finally taken photograph and analyzed. The microscopic anatomy of various pork livers in terms of central vein area, hepatic sinusoidal area, and zonal hepatic sinusoidal dilatation showed statistically significant difference between natural, Beta-agonist free, and hygienic pork livers. The microscopic anatomy of natural pork liver preferably presented the healthiest characteristic leading to the changeless of hepatic vasculature and zonation.

Keywords: pork liver, microscopic anatomy, food

1. INTRODUCTION

In Thailand, pork liver used to be a very popular food and also tend to be nutrient-dense superfood favored over other organ meats. A small amount of pork liver provides well over hundred percent of the recommended daily intakes for many essential nutrients which is also rich in high-quality protein and low in calories [1].

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Pork liver contains enriched vitamin B12 about three thousand percent of the recommended daily intakes leading to the healthy brain function and red blood cells formation. It also helps in vision, immune function and reproduction from the abundant vitamin A component [2]. The high amounts of copper in pork liver act like a key enzymes activator which plays important role in the regulations of energy production and iron metabolism. In addition, the benefits of folate and iron in pork liver also show dominant part in cell growth, deoxyribonucleic acid formation and oxygen carrying around the body, respectively [3]. In term of the body detoxification, liver is responsible for metabolizing drugs, hormones and medications. Moreover, liver also helps filtering wastes and toxins from blood prior to remove from the body [4]. The hepatic vasculature explains the circulation of liver that related to the hepatic blood vessels and homeostatic functions, in which the change of hepatic venous pressure are transferred quantitatively to the central vein and hepatic sinusoids [5]. Changes in hepatic blood flow also produce marked changes in hepatic clearance rates of a wide variety of compounds [6]. On the other hand, the hepatic zonation conveys the lined up of hepatocytes in a sponge-like arrangement between the hepatic sinusoids along the porto-central axis which shows a remarkable heterogeneity respecting to the maintaining of metabolic homeostasis via the biochemical and physiological functions [7]. As above-mentioned, liver is the one of representative vital organ in health status.

The main three various sources of pork liver are natural pork liver, Beta-agonist free pork liver, and hygienic pork liver regarding to the different farm types and treating methods. Natural pork liver is from the free-range swine which is treated in the natural range. The natural swine consumes clean water and clean food from the natural clean sources and free from Beta-agonists, antibiotics and chemicals [8]. Beta-agonist free pork liver is from the Beta-agonist free swine which is treated in the certified Beta-agonist free farm [9]. Hygienic pork liver is from the hygienic swine which is treated in the hygienic farm with free from Beta-agonists and diseases [10]. Even though, the three various sources of pork liver selling in the grocery stores have been certified by the Department of Livestock Development for their sources and qualities. Nevertheless, the differences in anatomical,

physiological and biochemical details of the various sources of pork liver have not been reported.

The microscopic anatomy of various sources of pork liver focusing on the hepatic vasculature and hepatic zonation were studied for the swine health status interpretation which supports the nutrient-dense superfood data of pork liver.

2. MATERIALS AND METHODS

2.1 Ethic statement

The current study was consistent with the Laboratory Animal Use Convention published by the National Institutes of Health. All animal experimental procedures were approved from the animal ethics committee of Center for Animal Research, Naresuan University (NUCAR).

2.2 Sample collection and histological analysis

Twenty-seven pieces of pork livers were bought from three different farm enterprises in Nakhon Pathom, Thailand: natural farm, Beta-agonist free farm, and hygienic farm.

Nine pieces of pork liver tissues in each farm were cut into 1x1x0.5 cm size and then fixed in 10% neutral buffered formalin for 72 hours, followed by tissue processing and paraffin-embedded. Three 3 µm thick sections were cut from each pork liver paraffin block in superficial, middle and deep parts by rotary microtome. All eighty-one tissue slides were Hematoxylin and Eosin stained, then mounted.

Five fields in all slides were taken photo by Olympus BX51 light microscope connected with digital camera, then recorded by ZEN 2012 (blue edition) program.

The characteristics of hepatic vasculature and zonation of five collected fields in all pork liver tissue slides were microscopically determined independently by two anatomists and one pathologist for qualitative and quantitative morphological evaluation to identify the hepatic zonation and hepatic sinusoid, and to quantify the area of central vein and hepatic sinusoidal enlargement. All parameters were measured and analyzed in 4X, 10X and 20X fields by the ImageJ program (https://imagej.nih.gov/ij/links.html).

2.3 Statistical analysis

SPSS 11.5 for Windows was used for statistical analysis. The quantities of pork liver microscopic anatomy including area of central vein, area of hepatic sinusoid, and zonal hepatic sinusoidal dilatation in three various sources were compared by one-way ANOVA method. The data in each experiment were calculated using mean ± SD. A p-value of < 0.05 was considered significant.

3. RESULTS

3.1. Hepatic vasculature of various pork livers

In order to determine the microscopic anatomy of various pork livers focusing on the hepatic vasculature, we performed Hematoxylin and Eosin staining to evaluate the areas of central vein and hepatic sinusoid in each kind of pork liver in 10X and 20X fields, respectively (Figure 1 and 2).

Natural pork liver, Beta-agonist free pork liver, and hygienic pork liver similarly had the hepatic circulation or hepatic vasculature. The liver receives blood from two sources including arterial and venous bloods. Arterial blood is furnished by the hepatic artery whereas venous blood is carried to the liver by the portal vein. The portal blood is laden with the products of digestion which have been absorbed from the gastrointestinal tract or alimentary canal and the digestive accessory organs by the portal vein to the liver where the metabolism occurring by the hepatocytes. Then, vein ramify like an artery, and ends in the hepatic sinusoids where the exchanging occur. After that, the blood again converges to reach the inferior vena cava via the hepatic veins.

As follows, the microscopic anatomy of pork liver presented as a lobule, roughly hexagonal arrangement of plates of hepatocytes and spaces of hepatic sinusoids radiating outward from a central vein in the center of hepatic lobules when observed in 10X and 20X fields. However, the characteristics and areas of central vein and hepatic sinusoid showed the statistically significant difference in three various sources of pork liver (Figure 1 and 2).

3.1.1. Central vein

The area of central vein was measured from the pork liver in 10X field (Figure 1). Central vein is the vein found at the center of hepatic lobules as presenting one vein at each lobule center, in which it is quite prominent in oval shape without the accumulated connective tissue on the border.

Natural pork liver, Beta-agonist free pork liver, and hygienic pork liver showed different area and characteristic of central vein. As the average of central vein area measurement, the size of central vein was statistically significant higher in Beta-agonist free pork liver and hygienic pork liver (82964.58 ± 12799.66 and 79996.88 ± 14765.10) when compared to natural pork liver (32650.13 ± 11233.12) at p-value < 0.001 (Figure 3). In addition, the central vein of natural pork liver showed the clear oval shape characteristic, whereas the enlarged size, irregular shape with the connective tissue accumulation around the internal border of central vein circumference were found in both of Beta-agonist free and hygienic pork livers (Figure 1).

3.1.2. Hepatic sinusoid

The area of hepatic sinusoid was measured from the pork liver in 20X field (Figure 2). Hepatic sinusoid is vascular space lined by a fenestrated endothelium without

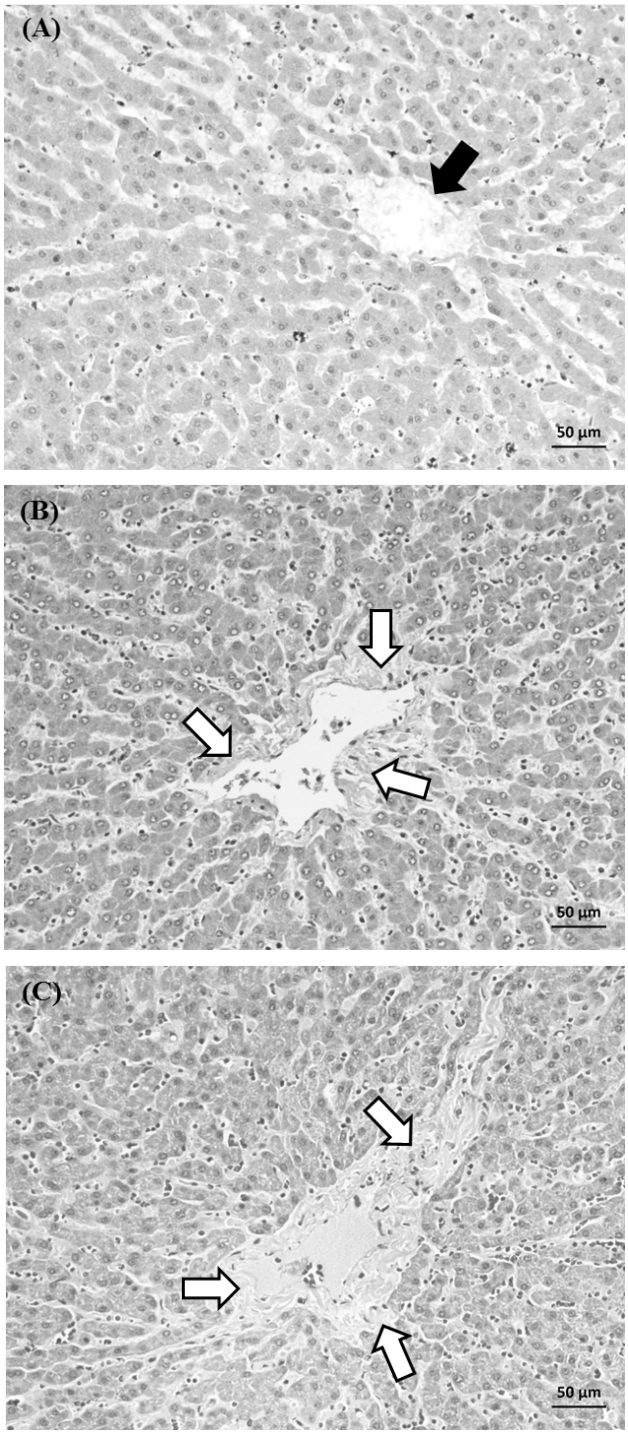

Figure 1. The central vein characteristic in various pork liver tissues, 10X field (n=9 each group): (A) natural pork liver, (B) Beta-agonist free pork liver, (C) hygienic pork liver. Note: black arrow indicates the clear oval central vein, and white arrow indicates the accumulation of connective tissue around the internal border of central vein circumference.

the basement membrane among hepatic cords, in which blood from both portal vein and hepatic artery mixes together in the hepatic sinusoids and then drains out of the lobule through the central vein which lining in the center. Therefore, hepatic sinusoid or space of Disse permits blood to percolate with hepatocytes. Normally, hepatic sinusoidal spaces are quite evident without the congested fluid or lysed red cells. This, in turn, provides appropriate space for efficient transfer of substances across the hepatocyte membrane.

Natural pork liver, Beta-agonist free pork liver, and hygienic pork liver showed different area and characteristic of hepatic sinusoids. As the average of hepatic sinusoid area measurement, the dilatation of hepatic sinusoid was statistically significant higher in Beta-agonist free pork liver and hygienic pork liver (34.92 ± 1.94 and 44.11 ± 2.79) when compared to natural pork liver (18.12 ± 1.54) at p-value < 0.001. The percentage of hepatic sinusoid area also showed the significantly higher in hygienic pork liver at p-value < 0.01 when compared to Beta-agonist free pork liver (Figure 4).

In addition, the hepatic sinusoid of natural pork liver showed the clear space containing few of Kupffer's cells between the hepatic cords, whereas the dilated hepatic sinusoid with many of inflammatory cell infiltration was found in both of Beta-agonist free and hygienic pork livers. Moreover, the congested hepatic sinusoid characteristic was also presented in hygienic pork liver (Figure 2).

3.2. Hepatic zonation of various pork livers

In order to determine the hepatic zonation of pork liver, we performed Hematoxylin and Eosin staining to evaluate the zonal hepatic sinusoidal dilatation lining around the hepatic lobule between the central vein and portal triad in each kind of pork liver in 4X field (Figure 5).

Natural pork liver, Beta-agonist free pork liver, and hygienic pork liver had regular hexagonal shape of hepatic lobule with central vein lining in the center, in which the hepatic sinusoids radially run between the hepatic cords of packed hepatocytes from central veins through the portal triads. The hepatic parenchyma is divided into three zones based on proximity to the central vein. Zone III is the area around the central vein, in which it is termed centrilobular zone. Zone I is the area closer to the portal triads which called periportal zone, whereas the area between both two zones is zone II or transition zone (Figure 6). However, the characteristics and zonal hepatic sinusoidal dilatation in all three zones showed the statistically significant difference in various pork livers.

3.2.1. Zone I (periportal zone)

The percentage of hepatic sinusoidal dilatation in periportal zone was measured from the zone I of pork liver in 4X field. The area of zone I or periportal zone is close to the portal triad (Figure 5). The result showed the statistically significant higher percentage of hepatic sinusoidal dilatation in hygienic pork liver (35.67 ± 1.34) when compared to the natural and Beta-agonist free pork livers (25.35 ± 3.11 and 26.13 ± 1.94) at p-value < 0.001 and p-value < 0.01, respectively (Figure 6).

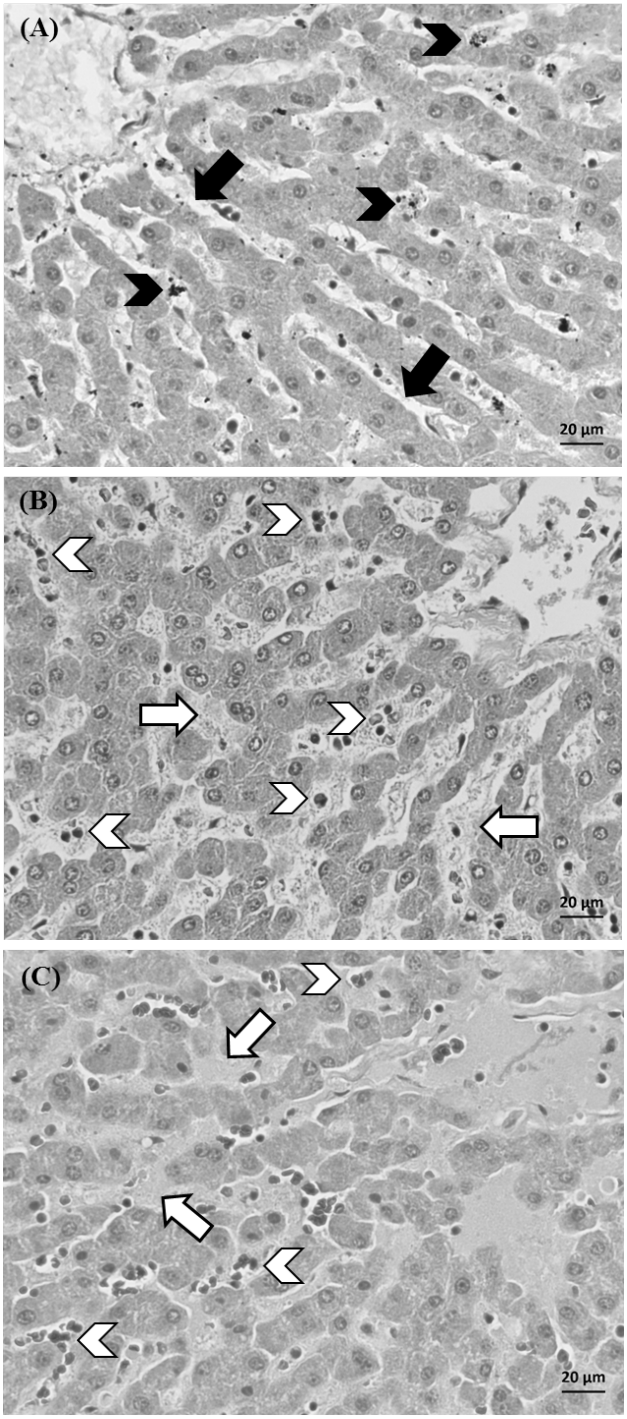

Figure 2. The hepatic sinusoid characteristic in various pork liver tissues, 20X field (n=9 each group): (A) natural pork liver, (B) Beta-agonist free pork liver, (C) hygienic pork liver. Note: black arrow indicates clear hepatic sinusoid, white arrow indicates congested hepatic sinusoid, black arrow head indicates Kupffer's cell, and white arrow head indicates inflammatory cell infiltration.

In addition, the zone I or periportal zone of natural pork liver showed the quite broad clear space of hepatic sinusoid between the regular packed hepatic cords when compared to other zones, however this is the narrowest space comparing to other various pork livers.

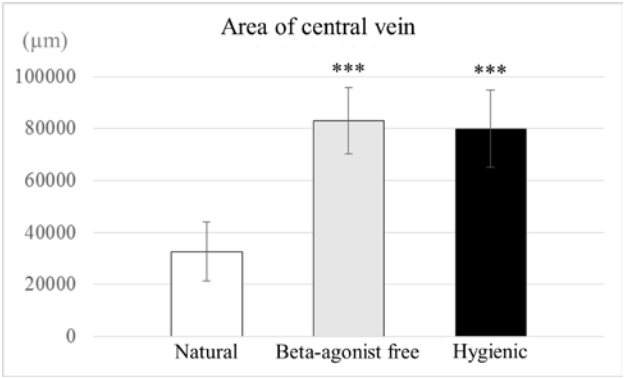

Figure 3. Area of central vein comparison between natural pork liver, Beta-agonist free pork liver, and hygienic pork liver (n=9 each group). *** indicates *p-value* < 0.001 compared with natural pork liver.

The zone I of Beta-agonist free pork liver also presented the quite regular space of hepatic sinusoid which lining between the rather swelling packed hepatic cords, whereas the congested dilation hepatic sinusoid between the swelling hepatic cords was found in hygienic pork liver (Figure 5).

3.2.2. Zone II (transition zone)

The percentage of hepatic sinusoidal dilatation in transition zone or midzonal zone was measured from the zone II of pork liver in 4X field. The area of zone II or transition zone is around the center area between the central vein and the portal triad (Figure 5). The result showed the statistically significant higher percentage of hepatic sinusoidal dilatation in both of Beta-agonist free pork liver and hygienic pork liver (27.50 ± 3.23 and 35.19 ± 2.57) when compared to the natural pork liver (12.17 ± 1.50) at p-value < 0.001. In addition, the percentage of zone II hepatic sinusoidal dilatation also showed the significantly higher in hygienic pork liver at p-value < 0.01 when compared to Beta-agonist free pork liver (Figure 6). Moreover, the zone II or transition zone of natural pork liver showed the mostly clear space of hepatic sinusoid between the regular packed hepatic cords, whereas the congested dilation hepatic sinusoid between the swelling hepatic cords was found in both of Beta-agonist free and hygienic pork livers (Figure 5).

3.2.3. Zone III (centriolobular zone)

The percentage of hepatic sinusoidal dilatation in centriolobular zone was measured from the zone III of pork liver in 4X field. The area of zone III or centrilobular zone is close to the central vein (Figure 5). The result showed the statistically significant higher percentage of hepatic sinusoidal dilatation in both of Beta-agonist free pork liver and hygienic pork liver (23.06 ± 1.52 and 29.05 ± 2.20) when compared to the natural pork liver (12.76 ± 2.88) at p-value < 0.001. In addition, the percentage of zone III hepatic sinusoidal dilatation also showed the significantly higher in hygienic pork liver at p-value < 0.01 when compared to Beta-agonist free pork liver (Figure 6). Moreover, the zone III

or centriolobular zone of natural pork liver showed the mostly clear space of hepatic sinusoid between the regular packed hepatic cords. The zone III of Beta-agonist free pork liver presented the quite clear enlarged space of hepatic sinusoid which lining between the regular packed hepatic cords, whereas the congested dilation hepatic sinusoid between the regular hepatic cords was found in hygienic pork liver (Figure 5).

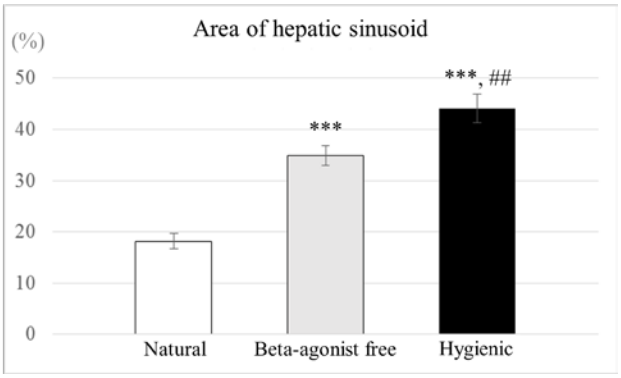

Figure 4. Percentage of hepatic sinusoid area comparison between natural pork liver, Beta-agonist free pork liver, and hygienic pork liver (n=9 each group). *** indicates *p-value* < 0.001 compared with natural pork liver. ## indicates *p-value* < 0.01 compared with Beta-agonist free pork liver.

4. DISCUSSIONS

Liver is the vital organ which plays many functions such as digestive enzymes producing, nutrients redistributing and especially in foods, drugs and also toxins metabolizing and detoxification [4]. All these functions lead it to be the essential organ connecting to the whole body. Liver injuries can affect overall health [11], therefore it is the one of health status representation. Alimentary tract is where nutrients and biochemical substances are absorbed through bloodstream, then raised and distributed to the liver [5]. The liver regulates the quality of nutrients and also creates antibodies to fight against the infections [12]. The crucial functions of liver can be limited by many factors which commonly involve in harmful substances perceiving [13]. In consequence, the different way of living might affect to the liver function, and also the liver characterization. In terms of the liver circulation, the hepatic vasculature is a dual venous and arterial circulation which is influenced by physiological and pathological processes within the liver. Hepatic vasculature alterations reflect hepatic metabolic adaptation and injury [5, 7].

Meanwhile, the hepatic zonation characterizes the metabolic pathways separation along the hepatic sinusoids within the hepatic lobules [7]. According to the anatomical structure of liver, it composed of a honey comb-like pattern of the hexagonal lobules arrangement by the hepatic cords and hepatic sinusoids lining. Hepatic cord, the hepatocytes lined up in a sponge-like organization between the sinusoids [5].

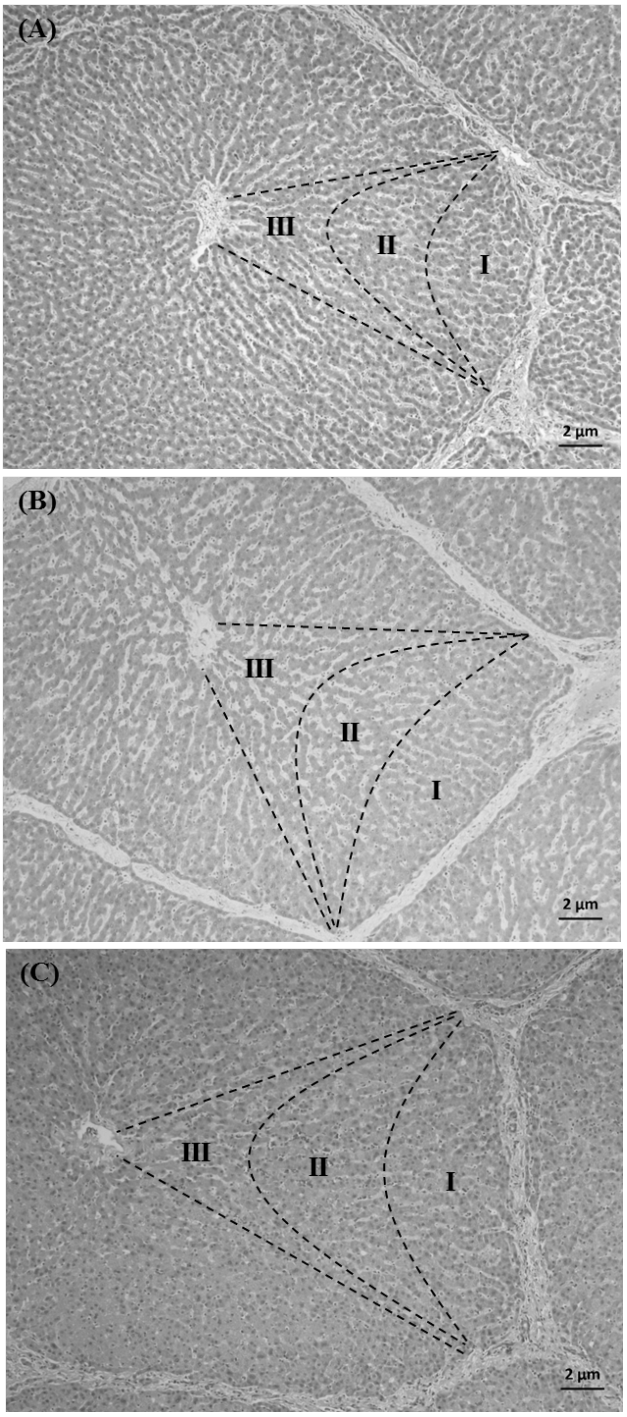

Figure 5. The hepatic zonation in various pork liver tissues, 4X field (n=9 each group): (A) natural pork liver, (B) Beta-agonist free pork liver, (C) hygienic pork liver. Note: I indicates area of periportal zone or zone I, II indicates area of transition zone or zone II, and III indicates area of centriolobular zone or zone III.

At the portal triad, the periphery of hepatic lobules consisted of hepatic bile ducts, hepatic venules and hepatic arterioles, in which blood from both vessels enter the anastomosing network capillaries which concentrically run to the central vessel called central vein. Then the blood from central vein drains into the hepatocytes along hepatic sinusoids in the hepatic venules [5-7].

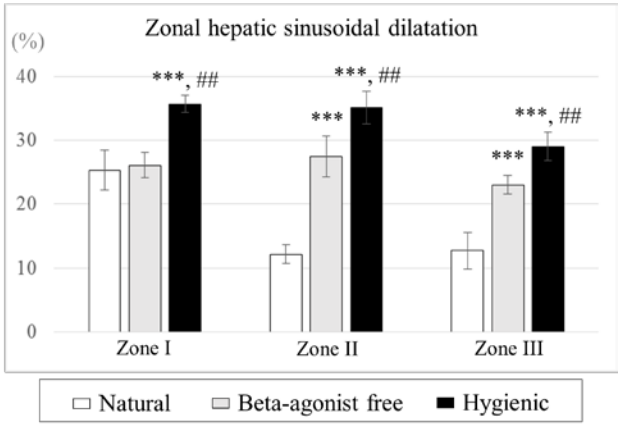

Figure 6. Percentages of hepatic sinusoidal dilatation in zone I, zone II and zone III comparison between natural pork liver, Beta-agonist free pork liver, and hygienic pork liver (n=9 each group). *** indicates *p-value* < 0.001 compared with natural pork liver. ## indicates *p-value* < 0.01 compared with Beta-agonist free pork liver.

Through the porto-central axis, the remarkable difference in biochemical and physiological functions were found, according to the heterogeneity in dynamic structural and functional known as metabolic zonation in which the homeostasis maintenance [14] and the liver function optimization [15] were reported as its potential. The inappropriate maintenance of metabolic homeostasis reasonably affects the hepatic zonation alteration [7, 14]. Either way, the alteration of hepatic vessels especially the central vein can also being caused by the implication of liver function [15].

To demonstrate the difference of health status in the various subsistence, we quantified the anatomical microscopic characteristic of liver in three various sources of pork including natural farm, Beta-agonist free farm, and hygienic farm by the Hematoxylin and Eosin staining in tissue slides, focusing on the hepatic vasculature and hepatic zonation.

In the view of hepatic vasculature in various sources of pork, we determined the characteristics and areas of central vein and hepatic sinusoid. The results presented the different finding in both vessel types when compared among three various sources of pork liver.

In general, natural pork liver, Beta-agonist free pork liver, and hygienic pork liver similarly had the hepatic vasculature or hepatic circulation. The liver receives blood from two sources including arterial and venous bloods. Arterial blood is furnished by the hepatic artery whereas venous blood is carried to the liver by the portal vein [5]. The portal blood is laden with the products of digestion which have been absorbed from the gastrointestinal tract or alimentary canal and the digestive accessory organs by the portal vein to the liver where the metabolism occurring by the hepatocytes [7]. Then, vein ramify like an artery, and ends in the hepatic sinusoids where the exchanging occur. After that, the blood again converges to reach the inferior vena cava via the hepatic veins [5, 7]. Considering at the center of hepatic lobule where the central vein located, the central vein of natural pork liver showed the regularly clear oval shape without the accumulation of connective tissue, and when compared to other two sources of pork liver, the smallest area was measured. In addition, the area of hepatic sinusoid of natural pork liver also showed the smallest percentage in which the clear space containing few of Kupffer's cells were observed. Normally, the hepatic sinusoid is vascular space lined by a fenestrated endothelium without the basement membrane among hepatic cords, in which blood from both portal vein and hepatic artery mixes together in the hepatic sinusoids and then drains out of the lobule through the central vein which lining in the center [7]. Therefore, hepatic sinusoid or space of Disse permits blood to percolate with hepatocytes [7]. In term of the natural pork liver, hepatic sinusoidal spaces are quite evident without the congested fluid or lysed red cells, similarly as the normal healthy status. This, in turn, provides appropriate space for efficient transfer of substances across the hepatocyte membrane leading to the homeostasis of the liver function [14, 15]. On the other hand, the area and characteristic of Beta-agonist free pork liver, and hygienic pork liver showed the dilatation of hepatic sinusoid containing many of inflammatory cell infiltration. Moreover, the congested hepatic sinusoid characteristic was also presented in hygienic pork liver. The central vein of both Beta-agonist free and hygienic pork livers also defined the enlarged size in irregular shape with the connective tissue accumulation around the internal border of the central vein circumference. The dilated hepatic sinusoids were reported as the characteristic of portal vein thrombosis, hepatic fibrosis, and Budd-Chiari Syndrome which caused from the portal hypertension [16]. Similarly, the hepatic sinusoidal congestion was found as the symptoms of the sinusoidal obstruction syndrome, which previously known as veno-occlusive disease [17]. These pathological characteristic appearances might present after drug or toxin exposure, together with the variable degrees of serum enzyme elevations and also jaundice and abdominal swelling signs [18]. Consequently, these anatomical microscopic characteristic of Beta-agonist free and hygienic pork livers might demonstrate the unhealthy status via the signs of hepatic sinusoid dilatation and obstruction.

In generally, three various sources of pork liver exhibited the regular hexagonal shape of hepatic lobule with central vein lining in the center, in which the hepatic sinusoids radially run between the hepatic cords of packed hepatocytes from central veins through the portal triads leading to the three areas of hepatic zonation [5]. The hepatic parenchyma is divided into three zones based on proximity to the central vein including centriolobular zone or Zone III, midzonal or transition zone or Zone II, and periportal zone or Zone I, respectively [7].

The hepatic zonation of natural pork liver displayed the lower percentage of hepatic sinusoidal dilatation in both centriolobular zone where located close to central vein and transition zone where located in the middle between the central vein and the portal triad, whereas the higher

dilated hepatic sinusoid percentage presented in the periportal zone where located close to the portal triad. Furthermore, periportal zone of natural pork liver showed the more quite broad clear space of hepatic sinusoid between the regular packed hepatic cords when compared to other zones. This presented the highly effective function of liver according to the porto-central axis lining. Blood enriched in oxygen supplied the higher rate in the area of Zone I where the hepatic artery located within the portal triad [19]. On the contrary, the metabolism rate together with the blood less in oxygen highly supplied in the Zone III where the central vein placed [19]. Hence, these zonal hepatic characteristics play the sufficient function in both nutrient and xenobiotic metabolisms and detoxifications [20]. In aspect of hepatic zonation in Beta-agonist free and hygienic pork livers, they presented the reverse characteristics with the natural pork liver. The higher percentage of hepatic sinusoidal dilatation was found in both of centriolobular zone and transition zone. The appearance of centriolobular zone in Beta-agonist free pork liver displayed the quite clear enlarged space of hepatic sinusoid, whereas the congested dilation hepatic sinusoid between the regular hepatic cords was observed in hygienic pork liver. The congested dilation hepatic sinusoid between the swelling hepatic cords was found in the midzonal zone or transition zone of both Beta-agonist free and hygienic pork livers. The congested dilation hepatic sinusoid in Zone III or centriolobular zone of hygienic pork liver might particularly regard as the perivenous hypoxia which interpreted as the reduction of delivered oxygen to the liver [21]. The previous clinical study reported that the perivenous hypoxia can be associated with perivenous damage [22]. The causes might be from the heart failure, obstructive lung dysfunction, sleep apnea or Pickwickian syndrome, gut ischemia, and also cases of drug hepatotoxicity [23]. These shifts of zonation may be brought about by hormones and other signaling molecules that regulated the physiological function of liver [24]. However, the reports of blood hormone or other xenobiotic level in the various sources of pork liver are important to strengthen these present findings.

5. CONCLUSION

This comparison of three various sources pork liver including natural pork liver, Beta-agonist free pork liver and hygienic pork liver in microscopic anatomy displayed the different in both hepatic vasculature and hepatic zonation appearances. The areas of central vein, hepatic sinusoid and zonal hepatic sinusoidal dilatation remarkably showed the pathological characteristics in hygienic pork liver. On the other side, the most normal characteristic of pork liver was found in natural source which might be interpreted as the normal functions of liver particularly in metabolism and detoxification. Therefore, the natural pork liver might be the choice of the nutrient-dense superfood leading to the healthiest manifestation properties. However, the needed further studies interest in the blood hormones or drugs detection for supporting causes of the normal and pathological microscopic anatomy in various sources of pork liver.

6. ACKNOWLEDGEMENTS

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