
Alcohol and Human Health in Viewpoints of Time

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Abstract: Evaluations of the effect of alcohol on human health are as old as alcohol itself. Opinions vary from the favourable, preventive and curative to the opposite, seeing alcohol as symbol evil, the scourge of mankind, toxic substance with a malignant effect on all organs. One of the most terrible is that by drinking even the smallest amount of alcohol, several thousand brain cells are destroyed. A creative person becomes a wreck. Seemingly contradictory views may not actually be mutually exclusive. This brings us to the concept of hormesis, which refers to the so – called biphasic effect, whereby a small amount of substance has a positive effect, but higher concentration of the same substance oppositely produced harm. *Dosis Sola Facit Venenum* - /The dose itself makes the Poison/ Paracelsus 1493-1541. In June 2nd, 1953 Slovakia honoured the coronation of Queen Elizabeth II by donating 50 litres of wine (Klevner- Pinot Gris) from Radošiná a village near to city of Nitra. Relevant committee deemed the *wine as excellent and worthy for the royal table on such a special occasion*. It was certainly not a poison.

Keywords: Bratislava Castle, Hormesa, Mouse Hill (Myšia Hôrka), Pompei

1. Introduction

Alcohol is a substance inherent to the human body, produced by the fermentation process in the metabolism of sugars, even in abstainers. This is evidenced by our genetic makeup, in which we find the enzyme alcohol dehydrogenase, by which is alcohol degraded. This is identical to cholesterol, which is synthesised in vegans, as it is an essential building block of every cell in our body, including brain cells. Cholesterol itself, belong to group of alcohol's as evidenced by ending terminal *-OL* in the name, confirming the presence of a *hydroxyl group in its molecule*. Alcohol is found such in fermented cabbage (sauerkraut) fermented cucumbers, raspberry and elderberry juice. Sweet fruits, honey dissolved in water, leavened dough, including bread, drink made from yeasted bread (*popular chlebnýj kvass in Russia*) acid milk products as kefir, yoghurt, koumiss. The amount of alcohol thus produced and ingested does not exceed a concentration of 0,1-0,2 per millilitre (g/kg) in our body and does not affect reaction time or the ability to drive a motorvehicle. Alcohol levels of 0,3 ppm (promile) or more are always the result of the consumption of a "real" alcoholic beverage. There is no lack of evidence of alcohol in any

known civilisation. [18] In the tombs of Egyptian pharaohs, evidence of wine has been found by modern analytical methods. Builders of pyramids ate daily garlic and drank beer. Confirmation of wine production was found in Mesopotamia, in the Mount Arrarat the place of the biblical Noah, the first wine grower and naturally in Palestine. The Jewish religion ranks both wine and alcohol as *healthy drinks*, with attribute of *ritual excellence*. There is *kosher wine*, but also *kosher slivovitz (plum brandy)*. However, wine is the king of drinks. A traditional Jewish wedding ceremony takes place under the wedding canopy (*Chuppah*), where the bride and groom standing, begin the rite by sipping the wine from a single glass, thus documenting their mutual future and shared destiny. At the heart of ceremony is the *Sheva Brachot* – seven blessings that are recited again over a glass of wine praising God and the value of family life, expressing the hope that happiness will accompany them on their life journey together. At the conclusion of the ceremony, the groom must break the glass as an image the fragility of life. Every week on Friday evening, at the set table with white tablecloth and two candles lit by the mother, the Sabbath begins with a blessing of *kiddush* wine, recited by the father of the family. At the end of the Sabbath on Saturday evening, perhaps still remembering the taste of the holiday shul, the father of

family ends the feast with blessing again over glass of *havdallah* wine.

Wine was predominantly red, including the Wedding at Cana of Galileo. (*The amount of water marvelously transformed to the wine was here roughly 600 litres*) To this day, virtually all grapes grown in Galilea were red. Tourist in this region can still buy a bottle of *Wedding wine* obviously in red. The true exception is the now modern vineyards on the Golan Heights.

The father of medicine Hippocrates of Kos (460-380 BC), is famous for the Hippocratic Oath, named after him, which thanks to its deontological balance, is part of the graduation ceremony even today's doctors of medicine. Hippocrates is famous for the saying: *Let food be yours medicine and medicine be yours food*. What was Hippocrates' attitude to wine? *Wine is wonderfully suited to man in health but also in sickness. However, it must be given in the right proportion according to the individual's physique i.e. individually.*

Pliny (Plinius) the Elder (23-79) was a Roman statesman, military leader, navigator and natural scientist. He was fateful for his direct observation of eruption of volcano Vesuvius which destroyed Pompei in August 79. Pliny suffocated by inhaling poisonous volcanic gases in nearby city of Stabia. Pliny was also a physician and wine was one of his favorite treatment tools. During archeological research at Bratislava castle, (Slovakia) traces of Celtic settlement have been found in area of north-western bastion since the 5th century BC. [24] Surprisingly here have been disclosed unexpected remains of Roman buildings from the 1st century BC, which according to the mosaic floors, the high quality of the plasterwork and its characteristic colour scheme, were built on the order of the Celts by the Romans constructors, the same ones who built the city of Pompei. Archeologists were assisted by high tech unique 3D computer reconstructions. (see appendix figure). In addition to the masonry buildings, wooden underground spaces used as cellars have been found. There were remnants of olive oil amphorae, but also of wine. The wine was excellent quality, originating from central Italy. The Roman legionaries on their expansion marches not only received a regular ration of wine, but also planted vines, founded vineyards and made own wine in the places of prolonged stay. As the Roman Empire expanded, viticulture gradually spread in this way. The famous inscription on the Trenčín (*Laugaricio*) castle rock from 179 AD, during reign of Emperor Marcus Aurelius and his son Commodus, is probably the northernmost evidence of Roman activity. The well-known Slovak enologist professor Fedor Malík, DrSc. states, that 300 years ago there were almost as many vineyards near Trenčín as in Modran famous Slovak wine producing district. [18]

Among the great personalities of science, who achieved decisive progress in the field of viticulture by describing scientifically verified procedures for the production of high quality wine was Louis Pasteur (1822-1895). Among his closest collaborators and followers was the Kharkiv-born, later Nobel Prize winner for phagocytosis, Ilya Ilyich Metchnikov (1845-1916) How did L. Pasteur evaluate wine?

"Wine is the most hygienic and healthiest drink." The veracity of this seemingly exaggerated claim was verified on 6 July 2010, when a gift from King Louis XVI of France (1754-1793) and his wife Marie Antoinette (1755-1793) daughter of Maria Theresa was found. The findings were recovered from the seabed at a depth of 50 meters off the Aaland Island in the Bothnic Gulf. The kings' gift was 30 bottles of the classic Champagne wine *Veuve Clicquot Ponsardin (Widow Clicquot)* intended for Russian Tsarina Catherina the Great (proper name Sofia Frederika Augusta von Anhalt Zerst). The name of Champagne wine was easily identified by the depiction of an anchor on a cork stopper. Both donors were publicly executed by guillotine in 1793 at the Place de Revolution in Paris. It is a cruel paradox that Louis XVI personally proposed an improvement in the shape of the execution axe, which was accepted with approval by Dr. Guillot himself. Champagne wine rested on the bottom of the sea since the Great France Revolution for 230 years! When the bottle was opened, the quality of champagne was evaluated as fabulous, pearled beautifully, had nice colour, excellent bouquet and great taste. It met all the chemical, microbiological and sensory criteria of the top highest quality. The secret was in appropriate quality of storage. At the depth of 50 m, the water pressure was 6 bar, the pressure inside the bottle is about 7atm, the water temperature is very stable at +4°C, the salty sea water has the highest density at this temperature, and at this depth it is practically completely dark. There were ideal conditions for perfect storage for Champagne wine, but no one envisaged such efficiency. Louis Pasteur was absolutely right!

Even with the finest and most exceptional wines, the question remains ultimately the same - *what is an appropriate dose of wine? When does this drink start to do harm?* [19] The answer to this complicated question was expressed by the Apostle Paul in his first letter to Timothy, 5/23: *Drink no more only water, but for stomach's sake, and because of frequent sickness, take a little wine*. A little in Greek *hemina=2,65 dcl*. This quantity became the basis for creation so-called Rule of St. Benedict, together with the well-known motto: *Ora et labora*. [18] It is therefore no surprise or coincidence that it was at the Benedictine Abbey of St. Peter in Hautvillers, region Champagne (France), where thanks to the innovative methods of the cellar master (cellerier) and local wine expert, Dom Pierre Perignon (1639-1715) a unique wine was created, according to the region with the appellation *Champagne*. At the beginning of the process was the blending (*assemblage*) of two blue vines Pinot noir and Pinot meunier, with white Chardonnay. A special pressing method, excluding maceration of the grapes, was used to produce a final white wine. The atypical pear-shaped bottles made of special thick glass, manufactured in these times in England, were better able to withstand the increased pressure inside in bottle. The cause of the increased pressure was secondary fermentation directly in the bottle. This process began by adding so-called "*liqueur de tirage*" composed from wine, sugar and yeast to each bottle and after this the bottles were provisionally sealed. Next was the

process of *remuage* rotation of bottles by hand in special racks and very slowly tilted downwards by the neck. Reason is the sedimentation from the process of fermentation put in the neck of bottle. The process lasted in deep cellars, with stable temperature, humidity and dark for 1-4 years. The end of this process is *degorgage after deep cooling of the neck of bottle*. Sediment after opening the seal shot out like a bullet. The missing volume from bottle was made up with expedition liqueur from wine and sugar. The absolute final is a seal of bottle with special shaped cork secured with a patent of Dom Perignon- from metal wire made *agraffa*. The classic Champagne wine is ready. In optimal condition, as in seabed in Botnick Bay his quality did not diminish. There is hardly a festive occasion on which this exceptional wine does not underline the importance of the moment. In every recommendation for serving wine, moderation is emphasised. An example is Heberden's description of clinical course of angina pectoris, together with advice on how to soothe the pain. In Heberden's time (1710-1801) nitroglycerin as remedy was not yet known. The first therapeutic action was to discontinue pain-inducing physical exertion, place the patient in a warm environment, or at least in a lee-side, provide mental reassurance, and the remedy of choice was a glass of wine or whisky. The vasodilating, antithrombotic and anodyne effects of alcohol were applied. Alongside the beneficial effects of alcohol, negative influence have always been described, especially when consumed immoderately. One of the most famous is the description of the *Munich Beer Heart (Münchener Bierherz)* published in 1884 by the pathologist Otto von Bollinger [1] He observed a group of men from Munich (Germany) with an extremely high beer consumption, averaging *432 liters per year*, which translated into consumption of more than *80g of pure alcohol/day, over period of 20 years*. The consequence was hypertrophy and later dilatation of the heart, ending in clinical picture of fatal heart failure. Today we might call this clinical entity as alcoholic dilated cardiomyopathy. Currently, beer consumption in Bavaria is 145 litres/year and German average is just over 100 litres/year. In neighbouring Czech Republic was last 142 litres/year and in Slovakia 72 litres/year. 7 There was also well-known affair in the 1960s in Quebec (Canada), where cases of cardiomyopathy attributed to drinking of a local beer, the "*Ale type*" (prepared by top fermentation). By analysis cause of cardiomyopathy was not the beer, but the addition of cobalt sulphate (CoSo₄) [4] which was supposed to improve the stability of beer foam. Cobalt, in small amounts is part of vit B₁₂, but in higher doses is very toxic, directly blocks mitochondrial dehydrogenases, affects membrane permeability and promotes the development of pericarditis. [4]. Cobalt itself does not belong in any form to beer preparation recipes. As early in 1516 *Wilhelm IV Duke of Bavaria* issued the first and oldest in beer brewing purity law (famous as *Reinheitsgebot*), which strictly ordered exclusively in preparation of beer: *water, barley, malt and hops*, and later also allowed the use of brewer's yeast. At the same time, it is the first *food quality law* to allow the use only

natural ingredients. The best quality breweries were established in monasteries. As the lower alcohol content of beer gave it the attribute of fasting beverage. Of course, quantity is also factor here. Wine as beverage was during fasting prohibited. A nice example of importance of quantity made Lian C. a military physician at the beginning of World War I (1915) [2, 3], monitored the blood pressure of group 150 french elderly soldiers aged 42-43 y in relation to the amount of wine they drank. In a group where the daily wine consumption was 3 litres or more (!) 25% of these had hypertension 150/100mmHg. If the daily wine consumption dropped to 2 – 2,5 litres, the incidence of hypertension also dropped to 17,5%. This is a confirmation that *quantity itself* is the decisive factor in the action of alcohol. [3]

The radical asceticism is mostly associated with protestantism and its typical features include total abstinence. The most powerful movement for prohibition was in the USA. However, one cannot help remembering that Martin Luther (1483-1546) author of 95 Theses, from Wittenberg, foundation of protestant reformation, as favorite beverage used Saxon beer. [2]

The strict alcohol prohibition movement in the USA reached Senate in 1919 and resulted in the adoption of the 18th Amendment to the American Constitution, which: "*Prohibited the manufacture, importation, transportation and sale of beverages containing more than 0,5% alcohol.*" It became law on January 16. 1920. There were exceptions for religious acts. The law also allowed doctors to directly prescribe 1 pint (about ½ litre) of liquor every 10 days on special forms. There were 27 indications in total for prescription of alcohol. e.g. *depression, even high blood pressure* ! The black market, high criminality, cottage industry of mostly very poor quality alcohol were all interfering disturbingly. On the positive side, there appeared to be a decrease in mortality from hepatic cirrhosis and a decrease in neonatal mortality. Other results were rather disappointing. Curiosities were also found, one of them being in the archives of British Prime Minister W. S. Churchill (1874-1965). Late in 1931 he signed a contract for a series of lectures, as partial compensation for the loss over 20,000£ on October 29 1929 (the Wall Street Crash) On 11.12.1931 he checked into Waldorf Astoria Hotel in New York and immediately rushed to railway station Grand Central Terminal to catch a train to Worcester Massachusetts, where he gave first lecture on 12.12.1931. On Sunday 13.12. after returning from Worcester, having dined at the hotel with his wife and daughter, he received an invitation to meet Bernard Baruch, financial adviser to American presidents and his personal friend, at 5 Avenue. He assumed that the hotel taxi driver knew the address. He didn't. After an hour of searching, Churchill getting nervous, stopped the taxi in the middle of the street and decided to walk to the other side himself. He hadn't gone 2 steps when a car pulled up on his right. Speed 35mph (56,3kmh) consequence: deep gash on forehead, another in back of head, broken nose, possible concussion, 2 broken 2 ribs, injury to both thigh. Numerous abrasions and blood bruising all over the body. Complication of rib fracture

was painful pleurisy with fever. He was discharged from Lanox Hill Hospital on 31.12.1931 in an invalid wheel chair, with a scar on his forehead, external fixation of his broken nose and swelling of his pale face. Chest pain persisted and mobility of both arms was restricted. Rehabilitation was dealt with in the Bahamas, the still a British colony. He swam in the sea, the weather was beautiful, there was no Prohibition and cars drove on the left as in London. His return to New York was January 25. 1932. The next day, 26.1.1932, Otto C. Pickhardt MD, 117 East Bow Street NY in his Office personally signed a typed statement, that *post-traumatic convalescence of W. S. Churchill necessarily required alcohol, especially at meals, and the total amount could not be defined, but he gave 250cc as minimum*. Doctor O. C. Pickhardt did not specify the type of alcohol. W. S. Churchill traditionally drank Pol Roger a classic dry French Champagne and Claret (a cuvée of dry red wines from Bordeaux) at meals. As early as January 28. 1932 W. S. Churchill gave a lecture at the Brooklyn Academy of Music. It was from Brooklyn that his mother came, in whose veins flowed a considerably of Iroquois blood. Apparently this fact also contributed to his amazing vitality. By February 21.1932 W. S. Churchill had given a total of 19 lectures, each in a different city. The honorarium reached 7,500£. On March 17. 1932 he was already being greeted by friends at Paddington station in London. Prohibition lasted until 5.12.1933 when it repealed after 13 years by another amendment to the constitution, by which time F. D. Roosevelt was already president and he welcomed the repeal of prohibition. W. S. Churchill was never a supporter Prohibition. He himself allegedly poured Johnnie Walker Scotch whisky into a glass in the morning, supposedly as a mouthwash.

In the fermentation process of making alcohol, its increased concentration begins to block the action of the yeast itself and automatically puts a brake on the fermentation process, preventing the formation of alcohol concentrations higher than 15%. The alcohol content can be increased by distillation. Methyl alcohol has a boiling point of 63,5 °C. Ethyl alcohol does not start to boil until 78,3°C and begins evaporate as vapour. If the alcohol vapour cools then precipitates and liquefies again, distillate is formed. Where and when first stills appeared is not entirely clear. The area of Mesopotamia-today's Iraq- is thought to be the area. When distillation stills came to us was a mystery. Not far from Spišský Štvrtok, with the Gothic chapel of the noble family of the Zápoľskis visible from afar, is the of Myššia Hôrka (*Mouse Hill*). As early as 19th century remains of 6600 m² guard fortress with the oldest walls made of dry-laid stones, a wide moat and left gate like in Greek Mycenae were found here. Bronze and gold jewellery with classical Mycenaean ornamentation, typical for the Ottoman culture were found here. The name Otomani is derived from place of same name in Transylvania in present-day Romania, which had close trade relations with Greek Mycenaeans. Among the various sherds stood out a ceramic vessel 34,5 cm high, which had special groove around the entire upper rim. It was preserved whole, only the cover part and purpose of this

vessel were mysteriously unknown. Modern analysis confirmed the age of oof the vessel to 1500 BC, the Bronze Age! [14] A similar, albeit larger and 2000 years older device has been found in central Meopotamia –today's Iraq. The purpose of Mouse Mountain vessel has been deciphered: it is a distillation device for the preparation of concentrated alcohol. (see figure attachment) Exceptional! Nothing like it has been found anywhere in the whole of Europe. [14] In Transylvania, in the town Maria Radna near Arad (Romania), the founder of the our, Third medical clinic Comenius University Medical school, academician TR Niederland, was born. His grandfather Petru Popovici worked there as tabular judge (judge of higher instance). He owned a large vineyard together with fruit trees. He always added wine and rakija to his workers in the vineyard along with Money. The local river Mureš regularly poured out of its banks, flooding the surroundings, the cellars of the house and also the water wells. The water was hygienically unsafe. Instead of water, the children and grandchildren were given wine, and grandfather kept the peace, he was a lawyer after all. Prof Niederland never condemned his grandfather's habit, no one in the became an alcoholic or teetotaler, including himself. He always knew peace. When the weather is clear, the view of the panorama of High Tatras from the Mouse Hill is beautiful. Our ancient ancestors probably did not chose this place at random. They felt awe respect and reverence for the mountans, sadly expressed by the humans sacrifices thatt have also been found at this archeological site.

2. Discussion

Food is intrinsic to life, not only as biological necessity, but food becomes part of the culture and a strong social factor that bonds family together. Its only a step towards honouring family members, honouring the food on the table. There is something particularly appropriate to this, a glas of wine. Wine has come to be accepted as a ceremonial and religious, also by diplomatic protocol. However, the question still resonated, is alcohol more beneficial or more harmful to the body. The results of 13-year long Prohibition did not provide a clear answer. Simple and complicated statistical methods, however had a fairly clear results: with the rising consumption of alcohol but also black coffeee, the incidence of myocardial infarction and strokes were significantly rising. Since these cardiovascular diseases were often found among the top political representatives (*e.g. US president Franklin Delano Roosevelt, he passed away because of hemorrhagic stroke in age 63*). From this reason there was a great social demand to create prospective epidemiological study to elucidate why these disease shorten the lives too early of those who might still be alive? Such study was find the place in city of Framingham Massachusetts, which met the criteria of an American-style urban life. [2] This city was close to Boston Mass, the headquarters of Harvard Medical School, which had expert oversight of the study. [12] The city of Framingham had a population of 28 000 at the time the study began, men and women aged 30 to 62 years who had no

evidence of cardiovascular disease and consented to undergo a medical examination every 2 years were recruited on a voluntary basis. In Wednesday 29 September 1948 was enrolled the first participant of the observation. As first study director was nominated Thomas Royle Dawber MD. The basic aim was to find out why heart and blood vessel disease manifested in one proband and not in the other looking for causal causes. At the beginning of the study, the general consensus was, that *drinking alcohol and black coffee were definite risk factors for cardiovascular disease*, the Framingham study was merely to confirm them. After 4 years, the number of volunteers had peaked at 5209, creating a baseline population large enough to allow statistically significant calculations. The expansion of the availability and quality of computing technology provided the application of state-of-the-art mathematical techniques that facilitate more accurate separation of causal relationship from confounding data. With the passage of time as the main criterion of truth, it finally crystallized that the risk factors for the development of cardiovascular disease are: Arterial hypertension, Tobacco smoking, Dyslipoproteinemia (*high LDL and low HDL. Higher HDL acquired value as favourable factor.*) Diabetes mellitus, Obesity, Sedentary lifestyle.

Drinking black caffeinated coffee even at a dose of *5 cups per day*, even at older age did not harm but, on the contrary, had positive effects, reducing both morbidity and mortality. Decaffeinated coffee had no such beneficial effects. Caffeine, belonging to the methylxanthines is a vasodilator, including of the coronary vessels. When caffeine is removed, the antioxidant potential of natural coffee which is virtually equal in magnitude to that of tea is impaired. Alcohol consumed in small doses reduced the risk of CVD disease, reduced the incidence of diabetes and improved glucose utilization by reducing insulin resistance. Alcohol reduced incidence of Alzheimer's dementia and Parkinson's disease. In alcohol, the original accusation were not borne out. [13] The beneficial effects, however were tied only to moderate, regular drinking with meals, to the exclusion of excessive, binge drinking. The explanation for the misinterpretation of the effects of drinking black coffee and alcohol as unequivocal pollutants lay in the underestimation of the unusually broad potential for toxic effects of smoking. Almost every lover of black coffee and alcohol was at the same time an avid smoker. Tobacco companies consistently blocked all information on the harmfulness of smoking that they found in their own laboratories. Publication was strictly forbidden. One cigarette produced 4750 separate toxic chemical components. There is no effective way to neutralise, filter or eliminate them. Noxious is smoking of pipe or cigars. Passive smoking is equally harmful and dangerous like so-called electronic cigarettes. (*F. D. Roosevelt was heavy smoker, seriously handicapped because of Polio (or Gulian Barré) he was on wheel chair, had sedentary and stressful duty, with very limited possibility of locomotion and improper relaxation, during the war-times, with symptoms of heart failure, with very high blood pressure without adequate treatment- his personal doctor was oto-rhinologist.*)

In 2006, the Institute of Lifestyle and Health at Boston Medical School and an International Center for Alcohol Strategy in Washington DC held an international symposium to assess the dangers and benefits associated with moderate alcohol consumption. It was noted that *alcoholic beverages are an integral part of culture* around the world. Moderate drinking has predominantly positive health effects. [8] Despite some disagreements in methodological approach, there is consensus on the inverse association between moderate alcohol consumption and the risk of cardiovascular disease but also diabetes mellitus, cognitive decline and overall mortality. On the other hand, there is undoubtedly an association between alcohol consumption and liver disease and some types of malignancy. It is almost exclusively a form of uncontrolled binge drinking without meals in uncultured environments. The culture itself represents and most effective agent for exclusion of harmful practices. However, it should be emphasised, that there is no safe dose for people with predisposition to develop alcohol dependence. Typical pattern is if father of family is alcohol dependent, his offsprings have very high probability to develop such dependency too. According to epidemiological studies, there is another importance – *the frequency of drinking* is more important, than quantity itself. More frequent drinking, including *daily drinking together with meal*, significantly *reduces risk*. Uncultured heavy drinking only one day of week on empty stomach, together with smoking, completely erases all positives of moderate drinking. In the search for mechanism of the beneficial effects of moderate drinking, the effect particularly on the rise in HDL cholesterol, esp. on HDL₂, HDL₃ subtypes, which affect endothelial function has been recalled, together with beneficial effects on platelet function, fibrinolysis and anti-inflammatory effects. [20, 21] Alcohol mediated increases in HDL, have important supporting mechanisms in the case of wine, particularly the red, where polyphenols and other powerful antioxidants are present. Red grape varieties are probably the indigenous ones. They are also most resistant to variety of pests. As late as second half of the 19th century, phylloxera (grape aphid) parasitic on the root of grapevines, spread epidemically from America to Europe. Hungarian wines had a high reputation. The polyhistor Matej Bel (1684-1749) was already responsible for this. He was native of Očová (near Zvolen), but he worked as evangelical parish priest in Bratislava. Many of his churchmen were wine-growers and so he had opportunity to taste the fruits of their labour. He especially appreciated the botrytic sweet fig-scented white wine of Svätý Jur (*St. George*) small city near of Bratislava. This kind *Viridula* produced *cibebs* with noble mould, like famous wines from Tokay region. *Viridula* was unfortunately not preserved thanks to Phylloxera. The salvation for the winegrowers was the use of so-called americanas as rootstock. The autochthonous varieties from America were all blue, naturally resistant to the disease of vines and did not require chemical protection. The protective substances in these vines are found in the skin and under the skin, and in order to get into the vine juice, the skin must be macerated. Maceration

also release the colour of skin into the juice, while the juice of blue grapes itself is colourless. (*An exception is kind Alibernet, which has also blue color of juice*) According to the archaeologist, the grape vine is older than man, growing in Mesozoic era about 150 million years ago. It is also genetically confirmed, that the ancestor of current vine species was blue. The emergence of white varieties is linked to a mutation in a gene for synthesis of the red pigment *anthocyanin* found in the skin of grapes. When breeding new cultivars during flowering, we have to wait 6 to 7 years after pollination for the grapes to mature and show their characteristics externally. The excellent breeder and author of many new grape varieties Ing. D. Pospíšilová, PhD. has exceptional results in this respect, awarded with gold medals from world wine competitions. New breeders from Slovakia are also gaining their place in the world's most sought in Michelin –starred restaurants. Wine is a natural source of a wide range of biologically active substances, the composition of which changes from year to year. It depends on the temperature, the number of sunny days, amount of nutrients in the soil, quality of the tillage, the amount of the natural moisture and the respect to agronomic deadlines. If a vine is threatened by e.g. mildew, it actively produces more protective substances. Opposite if the weather has been better for the vines, the amount of protective antioxidants is proportionally lower. It is often thought that only truly active component of wine is alcohol. [5, 15, 16], Juraj Harmatha of the Institute of Organic Chemistry and *Biochemistry* of the Czechoslovak Academy of Science in Prague provides a concise overview of this issue. [19, 20, 21]. In every wine there are free acids: *acetic, tartaric, malic, lactic, benzoic, salicylic*, phenylpropanoic acids: *p-coumaric, ferulic, caffeic*, some of acids are bound by combining with alcohol to form *esters*. Tannins among them mainly hydrolyzable and condensed tannins. Stilbenoids: *resveratrol* and its *dehydrooligomers- trans resveratrol, piceid, cis-resveratrol, resveratrol-trans-dehydrodimer, alpha viniferin, eta viniferin*, flavonoids: *quercetin, epicatechin, camferol, rutin*, lignans with *phytoestrogenic effect, nitrogenous substances, enzymes, vitamins and minerals*. The wine contains lignans which are converted to enterolignans in digestive tract. The presence of the hormone *melatonin* has been described in red wines, which explain the sleep-inducing effect of wine. The stilbenoids, in particular the aforementioned *resveratrol* and its derivatives, which are predominantly present in red wines, are of major interest. Among the white wines, *botrytic wines*, where the grapes have been attacked by the noble mould *Botrytis cinerea*, which causes the formation of *cibebs* (like resins) in which is high concentration of phenolic substances and high concentration of sugars. In Tokaj region, the *cibebs* are hand-picked into special vessels so-called *putni* with volume of 23kg and added to 136 litre *göncz barrel* up to 3 to 5 *putni*. Number of *putni* is on label of Tokaj wines as symbol of quality. Paradoxically, the higher the concentration of *cibebs*, the higher the concentration of sugar, but the lower concentration of alcohol, as the fermentation is inhibited by the higher content of sugar. The *cibebs* are covered with wine

from Tokaj region: *Furmint, Lipovina and Muscat Yellow*. Maceration of the *cibebs* takes 3 days, followed by pressing and successive fermentation by addition of special yeasts. After fermentation followed maturation in barrels for about 3 years in cellars in tuff, at the temperature of 10-12°C. The cellar walls are covered with the special mould *Cladosporium cellare* and this includes 90% relative humidity create unique conditions for create unique wine. After such an overview, it is unlikely that we would be inclined to believe that *alcohol alone* is responsible for all the wine's effects. Starting with Framingham study, led by father of statistical medicine Richard Doll in Oxford: the British Doctors Study lasting for 13 years, the Copenhagen City Heart Trial, all confirm that a small regular consumption of wine with food reduces the incidence of heart attacks, ischaemic strokes and also the incidence of type 2 diabetes, moderate alcohol consumption was also beneficial after first myocardial infarction (SHEEP) [22,] Italian authors have summarised extensively the numerous data on the effect of alcohol on cardiovascular disease, confirming the phenomenon of the "J" –shaped curve. In their work, they highlight the possible mechanism of this positive action, in particular the rise in HDL cholesterol, the decrease in platelet aggregation, the decrease in reperfusion injury, the increase in endothelium-dependent vasodilatation, the decrease in the activity of plasma coagulation factors, in particular f VII. Decrease in level of fibrinogen, increase in fibrinolysis, increase in atrial natriuretic peptide. It also fails to mention that moderate use of wine with meals is an integral component of the Mediterranean diet as an important means of improving the mood and decreasing social tension, together with cultural environment, nice cover and no plastic on the table. Mediterranean diet has been accepted by all major cardiological societies, but must be stressed that it is not only of proper composition and quality of food but much more. [23] Diabetes mellitus-2 has gradually transformed from rare to a common disease with in our country (*Slovakia*) of 7%. The major change is that the fate of these diabetic patients is predominantly determined by cardiovascular complications. The effect of alcohol was expressed by the terms of its action on development of diabetes has been investigated in numerous studies. Of 26 studies with a total 706 716 participants 275 711 were men, 431 005 were women, and diabetes mellitus was diagnosed in 31 621 probands. The effect of alcohol was expressed by comparison with abstainers. Those who drank 1 alcoholic drink/day had a 17% lower incidence of diabetes compared with abstainers. Those who drank 2 alcoholic drinks/day had 26% lower incidence of diabetes compared to abstainers. Those who drank more than 2 drinks/day had lower incidence of diabetes compared to abstainers, but only by 2%, which was no longer statistically significant. The delicate boundary between the beneficial effect of a small dose of alcohol its loss as the dose increases is marked with admirable precision. [9-11]. Alcohol, especially when consumed excessively over a long period of time, is associated with an increased incidence of cancer. It is entirely clear whether alcohol acts directly or as an additive

factor, in addition to the effects of other xenobiotics, different types of food and smoking. In terms of relative risk, there is a clear relationship between alcohol intake and cancer in the following order: oral cavity, oesophagus, larynx, female breast and colorectum. The fundamental question is the mechanism of carcinogenic action of alcohol. Alcohol as such (per se) is not mutagenic. Acetaldehyde- the first stage of alcoholic degradation is both a carcinogen and a mutagen, because it is capable of binding to DNA and to cellular proteins. Genetic polymorphism of alcohol degradation may cause the normal prompt degradation of acetaldehyde due to alcohol dehydrogenase 2 disorder to be slowed, acetaldehyde accumulates, thus amplifying its mutagenic effect. In Southeast Asia, where the prevalence of the risk genotype is high, the incidence of malignancy is also significantly increased in the presence of this variability. [23] One way to refine what makes the difference in red wine is to de-alcoholise the wine. Hashimoto M et al. evaporated alcohol from red wine using a vacuum and temperature of 40°C. They compared water, Japanese vodka, red wine and finally red wine de-alcoholized. Flow-controlled vasodilatation of the arteria brachialis was monitored by ultrasound. The result confirmed that red wine, even after alcohol deprivation, improves endothelial function by different mechanism than alcohol. [21]

In 2018 was published in the prestigious medical journal Lancet a paper: Alcohol use and global burden of disease for 195 countries and territories, 1990-2016. Systemic analysis. [6] The study was supported by the Bill & Melinda Gates Foundation. Gates is one of the richest people on the Planet, distinguished by his philanthropy, strict vegetarianism and principled abstinence, which he demonstrated on the visit Šamorín (*Slovakia*) in 2017 where he accompany his daughter Jennifer on horse jumping competition. Slovakia was not among 195 countries evaluated separately, nor did participate professionally. The conclusion of 26 years lasted study was, that alcohol is one of the leading risk factors for all disease. The risk of mortality from all causes and specifically cancer, rises with increasing alcohol consumption. [6] The authors found remarkable differences. In Nepal only 1,5% of women drink but in Nepal men drink 21%. In Sweden drink 86% women and 87% men. In 2016, globally drinking alcohol was 7th risk factor for premature death. In age range 15-49 years drinking is the number one risk factor by lowering immunity (e.g. causes tuberculosis) and in second place traffic accidents. One countries assessed was United Kingdom. There were 914 cases of cancer accidents registered in 100 000 abstainers. If 1 alcoholic drink per day (10g of alcohol) was added the number of cases by 4. If the number went up to 2 alcoholic drinks, the number of illnesses went up by 63. If the number of alcoholic drinks was 5, the number of illnesses increased by 338 compared to abstainers. In small amount of alcohol reduces a woman's risk of diabetes it is at expense of an increased risk of breast cancer. The most important news is that alcohol consumption that minimizes health losses is zero. *There no safe dose of alcohol.* Prof. D Spiegelhalter of Cambridge University adds *there is no completely safe way to drive a car. No government is going to impose a ban of driving.*

In 2018 a WHO Global position paper on Alcohol and Health was published. As the direct relationship between alcohol consumption and tuberculosis stands out from previous work, what is the WHO's stance on the issue. The WHO emphasizes that alcohol, *but in severe alcoholism* cause severe immune disorders an additionally interferes with the resorption of antituberculosis drugs. [7] In the case of cancer, the increased susceptibility of women is emphasized, recalling the modulating effect on estrogens. In the case of cardiovascular disease a protective effect on ischemic events is emphasized, but with exclusion of binge drinking. In liver disease, the importance of malnutrition as a supportive factor and the key role of metabolites in their degradation in liver are highlighted. Antidiabetogenic by way of improving insulin sensitivity along with the risk hypoglycaemia. As a preventive measure, first and foremost, the principle of never drinking fasting should be carefully observed. However excessive alcohol consumption disrupt glucose homeostasis, induces insulin resistance and increase the risk of diabetes. A serious problem is the combination of alcohol and psychoactive substances, which have a multiplicative effect on each other. Similarly with tobacco, where there mutually potentiating carcinogenic effects, it is true that immoderate alcohol consumption and excessive smoking are often combined. In its opinion, the WHO highlights the fact that improving the economic situation of the population also reduces risk of uncontrolled alcohol consumption. A logical annex to the WHO Global Position Paper on Alcohol, on p. 405, is Table IV.2, dividing the countries on the world by income level into 4 groups. [7] The table was prepared by the World Bank in Washington DC. It was also pleasant surprise for me that Slovakia was included in the first group with highest income, together with Czech Republic, Germany, Denmark, Switzerland etc. Consumption in liters of pure alcohol per person per year Slovakia in year 2011: 13,3 2016: 11,5 2018: 9,9 which puts Slovakia in the 15th place in OECD countries. According the WHO structure in 2016 the structure of kinds of alcoholic beverages consumed in Slovakia was created 42% by spirits, 34% by beer and 21% by wine. Trend of consumption was slightly changed: decreasing in spirits a slightly increased in beer. For illustration between OECD countries on the First Place is Lithuania, with the consumption of 13 litres of pure alcohol. Czech Republic and France had the same consumption 11,7 litres of alcohol, and occupied both second place. [7]

3. Conclusion

In April 2019 academic artist Stanislav Lajda from Žilina published 544 page monograph, *The Last Supper (Ultima Cena)* by Leonardo da Vinci together with a own reconstruction of Leonardo's famous wall paintings in refectory (*Il Cenacolo*) of Dominican monastery of *Santa Maria delle Grazie in Milan, Italy*. The original Leonardo's paintings is deeply deteriorated and S. Lajda spent more as 10 years on reconstruction of this work as his own expression of homage to this impressive opus of great master. [25]

Christ's famous phrase: *One of you will betray me*, suddenly appeared in amazing colour power. Each of Apostles of other dress in other dye glow, and striking distinctive face expression of a greatest astonishment. Judas had just scattered salt-cellar and salt sprinkled on the table, a nevil omen. A cup of red wine appeared in front of each of the twelve, in each in a different quantity. Today we are fully aware of the holy words: *Simili modo postquam coenatum est (in like manner, when supper was over) Accipite et bibite ex eo omnes (take and drink of it all of you)*. Along with Eucharistic dimension, we also accept the important profane component. Drinking *wine* should be *always after meal*, thus slowing down the breakdown of alcohol, acetaldehyde levels are easily broken slowly by alcohol dehydrogenase 2, thus minimizing the side effects. At same, the dose of wine is strictly individualized. On the other hand the challenge: *bibite ex eo omnes* is the gurantee, that the Master who said this most certainly not offering a highly toxic substance to His disciples.

Reports of the beneficial effects of resveratrol and some other wine bioflanoids have resulted in the development of various nutritional supplements. J Harmatha from the Czech Academy of Sciences in Prague commented on this: *No biological supplement can replace or ever surpass the truly natural, remarkably perfect, gastronomically pleasing, humanly refined, civilisation-phenomen and by centuries culturally anchored galenic form of quality wine.* [19]

For whom we do not recommend wine or any other alcohol beverages: Those who are at risk of developing an addiction- if they have a direct relative, especially a father who suffered from addiction. The caveat is the excellent tolerance of alcohol in *young ones*. No redness in the face, no heavy feet, no unsteady gait, no articulation problems. There is a deep feeling that the alcohol for "me" is a friend.

No recemendotion of alcohol for patients with neoplastic, or inflammatory disease of gastrointestinal tract, liver and pancreas disease. [17] Dangerous is concomitant us of psychoactive drugs with alcohol. When definitely not: naturally, pregnancy.

Dedication

Dedicated to the 100th anniversary of the funding of the Faculty of Medicine of Comenius University in Bratislava (1919-2019).

Appendix



Figure 1. Hypothetical 3D reconstruction of the interior of the "Roman Building I." research of M. Musilová, at Bratislava Castle [24].



Figure 2. Hypothetical reconstruction and view into the cellar with amphorae according to the research of M. Musilová at Bratislava Castle [24].



Figure 3. Distillation device (pot) from the Bronze Age (1500 BC) found at the urban-type hill-fort Myšia Hôrka in the cadastre of the village of Spišský Štvrtok (Slovakia). Ryšánek et al. [14].



Figure 4. Reconstruction of the distillation device (pot) from Tepe Gaura (north-west Iraq). Ryšánek et al. [14].

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