Antibiotic in Iraq's Animal Products and Feed-review

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Abstract

Any edible part of an animal product that has been given antibiotics will include trace levels of antibiotic residues, which are metabolites. Antibiotic resistance may arise as a result of antibiotic residues in food animals exceeding the permissible maximum residue level. Due to the widespread use of antibiotics in veterinary care, antibiotic residues may be found in a variety of animal-derived goods, such as milk, eggs and meat. These residues cause issues for the dairy and cattle industries as well as significant public health implications. The health risks associated with antibiotic residues in animal feed and products in Iraq are highlighted in this review. Strict adherence to safety standards is necessary to ensure that animal products do not include any illicit remnants when they are sold for human consumption. Veterinarians are the ones who must prescribe antibiotics. Growers and farmers must become more conscious. Implementing laws and regulations in this area aids in limiting the usage of antibiotics. Therefore, to control and prevent residues in food, producers, veterinarians, educators, academicians, marketing associations, and other interested parties should collaborate. Raising awareness of the issue through education about the drug's withdrawal period can also help.

Keywords: Antibiotic residue, Feed, Dairy product, Meat, Egg, Honey and health

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Introduction

Antibiotics are naturally occurring compounds that come from bacteria or fungi. Antibiotics also refer to substances that are created by contemporary chemical synthesis and biotechnology but do not exist in nature. Antibiotics are defined as chemicals that may either kill or prevent the development of bacteria. Antibiotic residues are a result of the widespread use of antibiotics in food that is regularly ingested (Bacanlı & Başaran, 2019). Antibiotics were shown to have a growth-promoting impact in the 1940s when it was found that animals given dried mycelia of Streptomyces tumefaciens containing residues of chlortetracycline had better growth (Castanon, 2007).

Thus, a ban on growth-promoting antibiotics has been recommended by the World Health Organization, the American Medical Association, and the American Public Health Association (Graham et al., 2007). Antimicrobial residues found in foods derived from animals coupled with noncompliance with use guidelines (dosage and waiting period) or subpar methods of raising cattle, can have detrimental effects on the health of consumers (Hsieh et al., 2011). The rise of resistant bacteria, or "superbugs," is attributed to the abuse of antibiotics in animals raised for food. These can result in severe disease when transferred to people. Antibiotic residues in food derived from animals raise two concerns: first, they may pose a direct hazard to human health; second, low levels of antibiotic exposure may change the microflora, lead to illness, and possibly result in the emergence of resistant strains that render antibiotic therapy ineffective (Dibner & Richards, 2005). The use of antibiotics in food, antibiotic residues in feed, and their effects on health are all significant issues that need to be taken into consideration in this review. For these reasons, the goal of this article is to review antibiotic residue control and preventive strategies in order to draw attention to the risk's antibiotic residue poses to public health.

Antibiotic and Antibiotic Residue

Antibiotics are medications that are used therapeutically to safeguard both human and animal health and wellbeing. Originally used to describe any biological agent that can harm living things, the term "antibiotic" is today used to describe compounds that have antibacterial, antifungal, or antiparasitic properties. Approximately 250 distinct chemical entities are now registered for use in veterinary and medical care (Kümmerer & Henninger, 2003).

Major Classes of Antibiotics

1. Beta lactams: Lactam antibiotics work by targeting the bacterial cell walls to cure illnesses caused by bacteria. They feature a -lactam ring nucleus with a heteroatomic ring structure, including three carbon atoms and one nitrogen atom. For example, amoxicillin, cloxacillin, ampicillin, and penicillin (Boucher et al., 2013).

2. Tetracyclines: These antibiotics are classified as "a subclass of polyketides having an octahydrotetracene-2-carboxamide skeleton" that are used to treat bacterial brood illnesses. Such as oxytetracycline, chlortetracycline, and tetracycline (Noel et al., 2012).
3. Macrolides: They are basic, lipophilic antibiotics that are used to treat infectious diseases in cattle, sheep, pigs, and poultry. They have a 14-membered macrocyclic lactone ring connected by glycosidic linkages, and they are effective against a wide range of gram positive and negative bacteria. Examples of such antibiotics include tylosine, erythromycin, and lincomycin (Sutcliffe, 2011).
4. Aminoglycosides: They comprise an aminocyclitol ring joined to two or more amino sugars by a glycoside bond and used to treat bacterial brood illnesses. Such as streptomycin, gentamycin, neomycin, and spectinomycin (d'Urso de Souza Mendes & de Souza Antunes, 2013).
5. Polymyxins: Polymyxins function by reacting with the cell membrane's phospholipids and rupturing it, which results in permeability and the death of bacteria. These substances are exclusively effective against Gram-negative bacteria. Since multidrug-resistant Gram-negative pathogens have emerged, there has been a revival in the systemic use of polymyxins, although their systemic usage is not advised owing to toxicity concerns (Goodman, 1996).

Antibiotics are mostly used in animals for three purposes: prophylactically to prevent infection in animals, therapeutically to treat sick animals, and as growth promoters to increase feed utilization and production. Because of their growth-promoting qualities, antibiotics are frequently added to animal feed at subtherapeutic levels (Okerman et al., 1998). Although numerous health issues in humans may be brought on by antibiotic residues in meals derived from animals. These issues include carcinogenicity (e.g., sulphamethazine, oxytetracycline, and furazolidone), mutagenicity, nephropathy (e.g., gentamicin), hepatotoxicity, reproductive disorders, toxic effects, the transmission of antibiotic-resistant bacteria to humans, immunopathological effects, and allergy (e.g., penicillin) (Nisha, 2008).

Interactions with gut microbial populations are a part of the mechanism of action of antimicrobial drugs as growth promoters (Dibner & Richards, 2005). Growth promoters are antimicrobials that, when added to animal feed in small amounts, can help prevent some bacterial infections and improve feed digestion by changing the makeup of the intestinal microbiota. Livestock growth is accelerated by these protective impacts on animal output (Baquero & Garau, 2010). Antibiotic residues are the parent antibiotics or their metabolites that are administered and end up deposited in animal tissues and animal-derived materials meant for human consumption when the concentration is higher than what is allowed for a specific amount of time (Nisha, 2008). Regular use of antibiotics may lead to drug residues that appear in animal-derived products like milk or meat at varying concentrations. The presence of antibiotic residues in food items may provide health risks to humans. These include bacterial resistance to antibiotics in microorganisms, sensitivity to antibiotics, allergic responses, microflora imbalances, and losses in the food business (Kempe et al., 1999).

Movements of Antibiotic Residues Through the Animal-human Interface

Before antibiotic residues are discovered in food, several things happen. We modified the conceptual model put out by. (Movement of antibiotic-resistant bacterial strains/genes between different ecosystems) because we judged that the movement of residues obeyed a similar dynamic (Figure 1) illustrates how human-animal contact, whether direct or indirect, has the potential to spread antibiotic residues. When antibiotics are administered to plants or animals and then become directly residual in the food after harvest or slaughter, this is known as a direct interaction. Conversely, indirect contact takes place when antibiotic residues from manure, which contains animal residues, or human excretions, which contain human residues, end up in food, particularly in vegetables owing to watering or animal feces contamination (Sharma et al., 2018). It is crucial to emphasize that the kinds and dosages of antibiotics given to the animals, as well as the method of administration, are critical factors in the direct process. It appears that injections are the primary way in which antibiotic residues above the requirements are provided among the various modes of administration (oral, parenteral, or topical) (Katz & Brady, 2000).

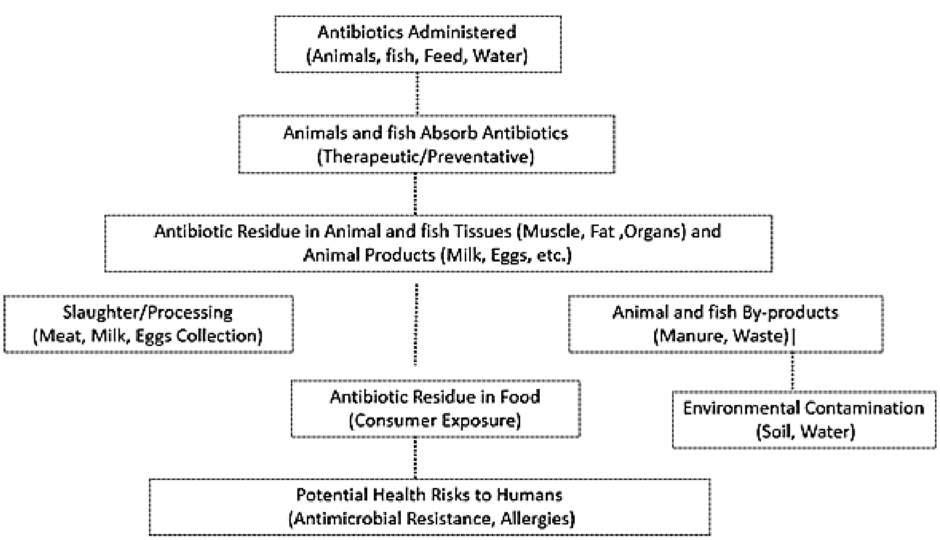

Fig. 1: Conceptual representation of possible movement of antibiotic residues between different ecosystems

Animal Feed

Iraqi probiotics are described as "live microbial supplements or components of bacteria and yeast," and research has indicated that they improve the well-being and productivity of animals (Hamasalim, 2009). The purpose of probiotics is to create a healthy microbial balance in the colon by combining helpful bacteria with animal feed which enhances animal performance, particularly in stressed animals that endure heat stress and consume unhealthy or poisonous food (Zinedine et al., 2005). Antimicrobial growth promoters (AGPs) are used to aid in better food digestion, maximize nutritional value, and support the development of robust, healthy animals. Antibiotics have a wide range of applications in the treatment of infectious illnesses in animals, including humans (Thakare et al., 2020). Drug resistance has gained its importance due to the transmission of antibiotic resistance factors to other enteric organisms which have posed a serious public health problem. Because antibiotics are readily available and reasonably priced, they are widely employed in the animal husbandry industry. The primary factors contributing to the issue are incorrect antibiotic usage and livestock producers' ignorance of antibiotic withdrawal times. Several public health organizations throughout the world view it as an unlawful practice when food derived from these animals has antibiotic residues exceeding the Maximum Residue Limits (MRLs) (Jayalakshmi et al., 2017). There is a need to make sure that antibiotics that are crucial to human health care are not administered therapeutically or preventatively to animals, and the continuous use of antibiotic growth promoters has drawn criticism.

Milk and Dairy Product

For more than 60 years, prevalent pathologies including mastitis, respiratory, and foot disorders, among others, have been treated with antibiotics in livestock care, both as a preventive measure and as a therapeutic intervention. 73% of antibiotic use worldwide is thought to come from the use of antibiotics in animals raised for food (Treiber & Beranek-Knauer, 2021). Milk comes from a variety of sources, including cows, buffalo, and camels. Moreover, milk comes in full-fat, low-fat, pasteurized, and sterilized varieties. Because different antibiotics are sometimes used indiscriminately to treat mastitis, there has been a reported incidence of antibiotic residue in milk products (Firth et al., 2021). All ages eat milk, although in varying quantities. Antibiotic-free milk is essential for both greater milk quality and the health of consumers. The economy will also be impacted by this. This is due to the fact that milk is not only drunk raw but also serves as the primary raw material for a large number of different dairy products. However, targeted preventative therapy is currently being researched and evaluated globally in herds with low levels of infectious mastitis issues because of rising worries about antibiotic resistance (Rajala-Schultz et al., 2021). Infectious foot disease and uterine and respiratory infections are prevalent infectious disorders in dairy cows. Lincomycin, β-lactams, tetracyclines, and sulfonamides are among the antibiotics used to treat foot infections. Treatments for metritis or respiratory illnesses typically involve the use of ceftiofur and other β-lactam antibiotics, tylosin, tilmicosin, florfenicol, tetracyclines, and sulfadimethoxine (Pol & Ruegg, 2007). The rise of antibiotic-resistant bacteria and the related health hazards have made the presence of antibiotic residues in milk a growing worldwide health concern. Antibiotic residues can have adverse effects including reduced acid production and milk curdling, as well as incorrect cheese ripening. Antibiotic contamination of milk or dairy products can cause anaphylaxis and upset the gut flora after consumption (Chiesa et al., 2020). There are two reasons to be concerned about antibiotic residues in milk. Initially, they might prevent cultured goods from properly fermenting lactic acid, which would lead to spoiling and possibly even the growth of staphylococci before the formation of curd. Second, if a person has already become sensitized to antibiotic contamination, consuming milk tainted with the bacteria might trigger a response. Antibiotic residues in milk can cause "allergic reactions, interference in the intestinal flora and resistance population of bacteria in the general population," among other possible risks (Althaus et al., 2003).

Meat Product

Antibiotic residues in meat are thought to pose a major risk to public health. The purpose of this study was to investigate the prevalence of antibiotic residues in mutton and lamb meat in Erbil (Almashhadany, 2020a). In the province of Duhok, a large number of animals are raised by herders who provide animal pharmaceuticals, especially antibiotics, in the wrong amount without a veterinarian's prescription and without knowing about withdrawal times (Yousif & Jwher, 2021). Because it contains a variety of nutrients, including proteins, minerals, lipids, vitamins, and trace amounts of carbs, among other bioactive ingredients, meat is regarded as a nutritious meal that may be included in a balanced diet (Odhaib et al., 2021). Beef that has antibiotic residues in it is thought to pose a major risk to public health. The phrase "antibiotic residues" describes molecules found in the flesh and organs of animals that have been killed and treated with antibiotics in the past but did not follow the drug's withdrawal time (Aidara-Kane et al., 2018). The majority of people are cautious when consuming meat from farms that heavily employ antibiotics throughout the manufacturing process. The fact that meat still contains antibiotic residues or their derivatives led to this cautious mindset. It is important to note that different antibiotics take varied amounts of time to leave the body. This length of time is known as the antibiotic withdrawal period (WP). The kind of antibiotic, dose form, and delivery technique all affect how long WP lasts. The withdrawal period must be respected during the antemortem examination of cattle since it might last anywhere from a few hours to many days or weeks (Al-mashhadany et al., 2018). The primary factors contributing to the issue are incorrect antibiotic usage and livestock producers' ignorance of antibiotic withdrawal times. Several public health organizations throughout the world view it as an unlawful practice when food made from these animals contains antibiotic residues over the Maximum Residue Limits (MRLs) (Jayalakshmi et al., 2017).

Egg

One of the major health problems is the presence of antibiotic residue in table eggs in Iraq country (Almashhadany, 2020b). Due to their high biological value of 93.7% and their high supply of necessary amino acids, eggs are a vital part of a balanced diet for humans. Protein makes up around 12.6% of an egg's edible portion. There are two sections in the internal edible core: the albumen (59%), and the yolk (31%). Most critical nutrients, including fat-soluble vitamins A, D, E, and K, and minerals required for physiological systems to operate properly, are found in the yolk (Réhault-Godbert et al., 2019). Because antibiotic resistance is becoming a more significant phenomenon, the presence of antibiotic residue in eggs is a contemporary concern. Although a chicken typically lays an egg every 24 hours, the in vivo development of an egg takes several days, and certain egg components persist for months before the fully mature and shelled egg containing them being deposited (Etches, 1996). Owing to the lengthy process of egg formation, it might take many weeks after treatment or exposure for eggs to be drug-free. Eggs containing folic acid may help prevent congenital conditions including spina bifida and macular degeneration, which is the main cause of age-related blindness. The buildup of lutein in the retina's fovea promotes eye health by absorbing harmful blue light (short wavelengths) and functioning as an antioxidant (Réhault-Godbert et al., 2019). Table eggs are susceptible to bacterial contamination from antibiotic residues much as other meals derived from animals. Antimicrobials are often employed in chicken farms as growth promoters to boost feed efficiency and as treatment agents for infectious illnesses. Antimicrobial residues (ARs) are the residues of antimicrobial agents that are left in tissues and eggs after the birds have been treated with them (Aidara-Kane et al., 2018; Stella et al., 2020). These medications enter the body through the colon, travel through the blood and/or plasma to the ovary, and end up in the oviduct's magnum. When the eggs plump up, the accumulation of ARs in the uterus, oviducts, and ampulla ultimately results in their inclusion in the egg albumen. Although several pharmaceuticals are permitted for other production classes of poultry, comparatively few drugs are marked for laying hens, which raises concerns about drug residues in chicken eggs (Castanon, 2007). Drugs that leave a laying hen's body quickly are likewise promptly expelled from the egg component a few days after withdrawal or treatment completion. Moreover, drug residue removal from egg components depends on the biological half-life of the utilized medication (Rana et al., 2019).

Honey

Honey is the naturally occurring sweet material that bees gather and store in their honey, which might be from nectar, bosom, plant excretions, or secretions of living things (Moore et al., 2001). Honey is a concoction of several substances and sugars. Honey mostly contains fructose (approximately 38.5%) and glucose (about 31.0%) as carbs making it comparable to inverted sugar syrup, which is made artificially and has around 48% fructose, 47% glucose, and 5% sucrose (Nhlapho, 2023). Additionally, honey includes trace levels of a number of substances, such as vitamin C, catalase, pinobanksin, chrysin, and pinocembrin, which are believed to have antioxidant properties. Yet the minerals are present in very small levels. The particular ingredients in each batch of honey are determined by the flowers the bees that made the honey could access (Al-Waili et al., 2012). The perception of honey is that it is a natural and healthful substance. But, the environment in which honey is produced nowadays is contaminated from a variety of sources. Both apicultural and environmental factors may be the source of contamination. Radioactivity, heavy metals, pesticides, and microorganisms are examples of environmental pollutants. Bees carry these pollutants to their beehives from the air, water, soil, and plants. Acaricides used to treat parasite mites (mostly Varroa), repellents for bees used during honey extraction, insecticides for controlling wax moth and tiny hive beetles, and antibiotics are some of the contaminants from beekeeping practices (Bogdanov, 2006). The main reason honey contains antibiotics is because apiculture uses them to treat bacterial illnesses. Oxytetracycline is often used to treat European foulbrood disease (EFB) and American foulbrood illnesses (AFB) caused by Paenibacilus (Bacillus) larvae and Streptococcus pluton bacterium, respectively. Tetracycline is still widely used, however due to resistance in these bacteria, there are now reports of it (Savarino et al., 2020). The principal mineral elements included in honey are K, P, Mg, Al, Ca, Na, Fe, Mn, Cu, Zn, Cl, S and Si. In terms of metabolism, health, and illness, trace elements are significant and essential. Although it is crucial that they are present in human meals, if their quantities are exceeded, they may be hazardous (Watts, 1990).The concentration of microelements can cause toxic danger, including heavy metals in nutritional products. This small amount of toxic heavy metals in honey bees is related to most bees or food contamination area in which they live, where contaminated bees that fly long distances also for tools that are used in the process of storage may be contaminated. Heavy metals are hazardous because, first of all, they do not break down during food processing; rather, their concentration increases as a function of mass unit. Second, because metals have the ability to accumulate within the human body, they can impede or even completely stop intracellular biological reactions. Thirdly, most metals have properties that make them carcinogens and mutagens. It is quite difficult to extract them from the human body after they have been digested (Zajdel et al., 2023).

Health Impact

Due to residues in food and raw materials derived from animals, the unrestricted use of antibiotics during animal raising may cause issues. Due to the effects that antibiotics have on aquatic life, human health, and water quality, their presence in Iraq's aquatic environment is extremely concerning (Ghimpețeanu et al., 2022). Drug residues in foods derived from animals may have direct negative impacts on human health, or they may have an indirect effect by spreading human pathogens through the selection of antimicrobial resistance determinants. Subchronic exposure levels have the potential to cause toxicity, carcinogenic effects, and allergy responses in susceptible individuals. If a large concentration of residues from penicillin remains in milk drank by those who are sensitive to the antibiotic, allergies may be caused, particularly by penicillin and other beta-lactam antibiotics like cephalosporin. Young children's teeth may potentially become stained by tetracycline residue (Phillips et al., 2004).

Drug resistance development: Humans can come into direct contact with resistant microorganisms or indirectly through milk, meat, and/or eggs. Due to their animal origin, these bacteria have the potential to either colonize human endogenous flora or contribute more resistance genes to the reservoir of genes already present in humans. Resistance transmission from animals to humans is a possibility. The development of human antibiotic resistance has been linked to the use of antibiotics in cattle agriculture. It is known that eating animal-based food can cause humans to get drug-resistant germs including Salmonella, Campylobacter, and Staphylococcus (Landers et al., 2012). Avaoparin and fluoroquinolones are two medications that have been demonstrated to promote the formation of resistant microorganisms in animal-derived foods. The WHO recommends that the subtherapeutic use of antibiotics such as penicillin, tetracyclines, and sulfa medicines, which leads to the development of bacteria with resistance, be given top attention in agriculture (Sundlof et al., 1995). Discharge of industrial wastewater, animal husbandry, municipal wastewater, and antibiotic disposal leachates from landfills. Runoff from urban areas, aquaculture ponds, and agricultural fields holding livestock dung are possible additional sources. Daily environmental exposure to antibiotic residues may cause a significant number of bacteria to enter the human gastrointestinal system, home to over 7000 distinct strains and 800-1000 distinct bacterial species (Jernberg et al., 2010).

There are two main concerns with the use of antibiotics in animals and their potential effects on human health: the kind of antibiotics used and their application methods. There is a belief that antibiotics, which are crucial to human health, shouldn't be medically administered to animals raised for food, especially when large quantities of the drug are involved. Two issues with prophylactic usage arise: the antibiotics utilized and the lack of knowledge on the proper period of prophylactic use. The use of antibiotics for growth-promoting purposes is perhaps the most concerning because some of these drugs are now thought to compromise the effectiveness of important human antibiotics, and the period of therapy may last the animal's whole life (Phillips et al., 2004). The concept of cross-resistance is highlighted by the data generated concerning bacterial resistance in cattle breeding and its relationship to human health. The connection between antibiotics used for human health and those used for animal health accounts for this phenomenon (Sharafat et al., 2023). Additionally, this issue is exacerbated by two primary variables. First, the agricultural and pharmaceutical sectors' fast and large-scale production became the center of economic interests. Second, consumers' and producers' ignorance about the constitution and the negative effects of antibiotics on human health when used improperly can result in allergic responses and fatalities from uncontrollable infections. This is especially true for small farmers (Oliveira et al., 2020).

The antibiotic itself or one of its secondary metabolites may leave behind residue. These materials can lodge, build up, or be kept in tissues, cells, organs, or foods that come from animals (Sharafat et al., 2023). The primary intent of administering these medications to animals is either to boost output or to prevent, manage, or cure animal illnesses. But with time and with consumption, these residues can build up in people, enhancing the selectivity of multi-resistant bacteria to these commonly used medications for human health (Riviere and Sundlof, 2001). Antibiotic residues in food derived from animals are one of the main things that should worry people's health. Ingesting these residues may cause a variety of problems, including direct toxicity, allergic responses, and cancer-causing consequences (e.g.: sulfamethazine, 4-dedimethyl amino-4-oxo-tetracycline and furazolidone), mutagenicity, nephropathy (e.g.: gentamicin), hepatotoxicity, reproductive disorders, bone marrow toxicity (e.g.: chloramphenicol), allergy (e.g.: penicillin), The eradication of beneficial bacteria found in the digestive system, particularly in young people, the elderly, pregnant women, and people with weakened immune systems (Nisha, 2008). Antimicrobial resistance can lead to a significant multiplication of "super bacteria" since new antibiotics are not being developed, which might eventually reduce or eliminate the possibility of treating illnesses caused by such multi-resistant organisms. Additionally, impulsive intake of these agricultural goods and the careless use of growth boosters in the development of products with animal origins might transfer those microorganisms from meals, mostly from animal sources, to the user (Tasho & Cho, 2016).

Conclusion

Veterinarians are the ones who prescribe antibiotics in need. Growers and farmers must become more conscious regarding antibiotics use. Implementing laws and regulations in this area aids in limiting the usage of antibiotics. Regular veterinary check-ups are advised to ensure that, if an infection is identified, early treatment is administered precisely within the withdrawal times, rather than delaying treatment until later in the infection cycle. The use of antibiotics in excessive dosages as growth promoters must be outlawed. To ensure the safety and quality of food in the local market, imported goods need to be continuously tested. Additionally, it is crucial to inspect food products to make sure that no prohibited antibiotics have been added, especially to milk samples in an attempt to extend their shelf life. Current surveys that are distributed to most people must be used to assess the exposure. The quantity of food consumed and the body weight should be the basis for calculations. Research needs to be updated often since several variables might affect the safety and quality of food, such as consumption patterns, illnesses, and climate.

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