



Review Article

HUMAN ECHINOCOCCOSIS: A REVIEW

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Abstract

Cystic echinococcosis, Cystic hydatidosis, hydatidosis, unilocular echinococcosis unilocular resulting from infection with the larval of *Echinococcus granulosus* is one of the most serious parasitic zoonotic diseases to humans and animals which suffered from humans since ancient times and to this day was referred to the disease for the first time in the Bible Talmud. The *Echinococcus* has an indirect life cycle requiring two hosts, the final host in which the parasite reaches puberty in the small intestine of carnivores of the Caniidae family including dogs, wolves, foxes, jackals, and hyena. The second host is called the intermediate host, in which the parasite proliferates in the organs and tissues of animals such as herbivores, sheep, goats, camels, horses, pigs, elephants, rabbits, kangaroos, monkeys and humans. In this review article, important information about the parasite that causes this disease will be mentioned, such as General description of Parasite, Historical background, Life cycle classification, Structure of Hydatid cyst, Pathogenicity and Clinical diagnosis methods and Treatment methods.

Article History

Received : 17.10.2020

Revised : 12.11.2020

Accepted: 10.12.2020

**Keywords:** Human echinococcosis, *Echinococcus granulosus*, Hydatid cyst, Pathogenicity, Clinical diagnosis and Treatment.

1.Introduction

The disease is similar to a bladder filled with water seen in the liver and lungs of sheep and cattle (Wang *et al.*, 2001; Nasrieh and Abdel Hafez, 2004; Dvorak *et al.*, 2008). The first case of cystic sacrosis was described in 79 - 460 BC by Hippocrates, which he described as a water-filled liver when observed in the liver of one of the deceased and stated that the explosion in the abdomen leads to the death of the patient.

The animal nature of the cystic sacs was first recognized by Fransisco Redi in 1684. Thus, aborting the theory of spontaneous reproduction. Hartmann was described as adult worms in the intestines of dogs in 1695. In 1773, Jone Hanter described the neural bags as circular structures containing a cavity filled with a pure white liquid (Mehlhorn, 2008), In 1782, Goze was able to diagnose the protoscolex of the cerebral sac in the liver of sheep, indicating that they were Granulating in the inner side of the cyst. He pointed to the similarity between their scolex and scolex of worms *Taenia* sp. called *Taenia visceralis socialis granulosis* (Thompson and McManus, 2001; Cook, 2001). Batsch was

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described as adult worms in the intestines of dogs in 1786 and called it *Hydatigena granulose*. In 1852, Vonsiebold was able to detect adult worms in the intestines of the dogs after three weeks of experimental feeding on hydatid cysts taken from cattle. The relationship between cystic larvae and adult worm was thus clarified (Muller *et al.*, 2007). The term Hydatid is the Greek word *Hydatid* (*Hydatid*), meaning water vesicle. It is derived from the modern Latin word *Hydatid*, meaning the drop of water. Hydatid cyst is still widely used in medicine (Moringlane, 2003; Milicevic, 2006; Craig and Larrien, 2007).

## 2. Classification of Parasite

Based on the description of Harder and Mehlhorn (2008), the location of *Echinococcus granulosus* can be described in the taxonomic system as follows:

Phylum: Platyhelminthes  
 Class: Cestoidea  
 Sub-class: Eucestoda  
 Order: Cyclophlidae  
 Family: Taeniidae  
 Genus: *Echinococcus*  
 Species: *granulosus*

A number of researchers have described 16 species and 13 sub-species belonging to the genus of *Echinococcus* depending on the type of work and the morphological and structural characteristics of the parasite (Thompson, 2008): *Echinococcus granulosus*, *Echinococcus multilocularis*, *Echinococcus oligarthrus*, *Echinococcus vogeli*, *Echinococcus longimanubrius*, *Echinococcus cruzi*, *Echinococcus ortleppi*, *Echinococcus camerani*, *Echinococcus fellidis*, *Echinococcus lyaonti*, *Echinococcus minimum*, *Echinococcus patagonicus* and *Echinococcus intermedius*. However, four species are important in taxonomic terms and these are: *Echinococcus granulosus* (Batsch, 1786), *Echinococcus multilocularis* (Leuckert, 1863), *Echinococcus oligarthrus* (Diesing, 1863) and *Echinococcus vogeli* (Rausch and Berustein, 1972). These species are distinct in

the adult phase and the larval stage, and their larval stages cause various forms of hydatid cysts in intermediate and occasional hosts (Morar and Felman, 2003; Schantz, 2006). In China, a new species was discovered and the larval and adult were distinguished. The Tibetan fan served as a final host and the Pika, as an intermediate host was named *Echinococcus shiquicus*. (Xiao *et al.*, 2006; OIE, 2008). Four sub-species belonging to *Echinococcus granulosus*, the most prevalent in Iraq, were identified as *Echinococcus anadensis*, *Echinococcus boreilis*, *Echinococcus quines* and *Echinococcus granulosus* according to form and vitality (Sweatman and Williams, 1963). Most of the researchers reported that there were differences between the strain of horses, cows, sheep, camels, and goats, while they found a similarity between the shape of the human infection and the shape of the infection in the sheep. This resemblance led to the adoption of only sheep strain in human infection.

## 3. General Description of Parasite

All species of *Echinococcus*, including *E. granulosus* are the smallest tapeworms that parasitize on predators in their adult stages and on the intermediate hosts including human in its larval stage. Dogs, wolves, and foxes are final hosts of this parasite (Dandan *et al.*, 2007). The length of the worm is between 3 - 11 mm and width of 0.5 - 1 mm and has 3 - 7 proglottids of body. The body is divided into three parts:

### a) Scolex

The pearly shape has a diameter up to about 0.3 mm and has a rustellum surrounded by two rows of hooks ranging from 40 to 28 spines with different lengths and reciprocal rank (ranging in number from one row to 28 - 50 hook). There are also a number of cells under the anterior end of the rustellum that secreted a sticky substance, that is not known to function (Bhamrah and Juneja, 2001; Muller and Wakelin, 2001).

### b) Neck

It is narrow and short-lived behind the scolex and is a reproductive zones with the ability

to produce new proglottids continuously (Wernery and Kaaden, 2002).

### c) Proglottids

Ranging from 3 to 7 proglottids and are found in three different types of size and maturity. The first proglottid which follows the neck is short and contains immature genitalia with a dark patch of cells called immature proglottid (Thompson and McManus, 2001). The second piece is called mature proglottid, which contains mature reproductive organs and are larger than the first and have a rectangular shape located in the middle of the genital opening, as well as containing 45 - 65 spherical testicles spread on the front side of the proglottid female genitalia consist of a single ovary located on the back with two irregular lobe in shape and Vitelline gland is located behind the ovary (Tunaci *et al.*, 1999). The third is called the gravid proglottid, the largest body piece, which is longer and wider and represents about half the length of the body and the uterus, which is characterized by the form Sac-like and non-irregular of the presence of 12 - 15 side by side and contains the limits of 500 -1000 eggs, the gravid proglottid separate from the worm and the eggs thrown out with feces (Muller *et al.*, 2007).

### 4. Eggs of Parasite

The eggs are oval shaped at a diameter of 30 - 40 microns, surrounded by a thick shell, like the rest of the tapeworm eggs belonging to the family Taeniidae, which cannot be distinguished from them in form Khuroo (2002). It also has resistance to environmental conditions for a long time and is out of the body. If it keeps its susceptibility to infection for a year if appropriate environments, but die if exposed to direct sunlight for at least ten hours. The eggs contain a Hexacanth embryo, a full-grown ovoid with a diameter of 25 microns and armed with three pairs of hooks (Muller *et al.*, 2007). The hexacanth embryo is surrounded by membranes and is from the inside out

- Capsule
- Layer vitelline
- Outer embryophoric membrane
- Embryophore

- Basal membrane of granular layer
- Oncospheral membrane
- Cimiting membrane

### 5. Life cycle of Parasite

The *Echinococcus* has an indirect life cycle, requiring two hosts, final host and intermediate host (Filippou *et al.*, 2007). The eggs that are released after the separation of the proglottids are the infectious stage of the intermediate hosts, where the eggs are given with a quantity of uterine fluid, which helps to stay alive for a period of time as well as the nature of the membranes surrounding them and make them resistant to high climatic conditions (Roberts and Janovy, 2000). The infection of the intermediate host is caused by the ingestion of contaminated fertilized eggs of herbs, vegetables and water. These eggs are hatched in the small intestine of the host from hexacanthus embryo which represents the first larval stage, which is active in the stomach and small intestine under the influence of enzymes Proteolytic enzymes including Pepsin, Pancreatin and Bile salts (Kelly and Kern, 2004). Oncosphere is characterized by the presence of Penetration glands as its secretions help to protect the embryo from digestive enzymes digestive and immune response of the host (Naguleswaran *et al.*, 2006). These secretions also work with the help of hooks on the penetration of the embryo mucoid layer located in the small intestine in 30 - 120 minutes (Crompton and Savioli, 2006). Then, the vascular channels penetrate and pass through the blood or lymph to reach the liver within three or four hours (Kuntiz and Kuntiz, 2006). The liver is the first filtration for the embryos of the hydatid cyst where large numbers of them are held, the rest of which passes through to the lungs, which represents the second filtration, holding fewer embryos. A small number of embryos go through the capillaries in the lungs to reach the systemic cycle, through which they reach different organs and tissues of the body such as spleen, kidneys, heart, brain, bones, etc. (Gurbuz *et al.*, 2006).

The incidence and distribution of the disease varies according to host and age. In

humans, the liver is the most susceptible to the disease by 65 – 71 % because it represents the first refiner of the body followed by the lungs by 25 % and 10 % for the other organs (Pawlowski, 1993). In 4 to 7 days, embryos become a typical bladder with a germinal layer forming non-cellular plates within 10 days. The diameter of the sac grows at a rate of 4 mm per month within the *in vivo*. This also occurs within the intermediate host and the condition changes from one host to another (Eckert *et al.*, 2001).

Infection to the final host through feeding occurs on the organs of the intermediate host infected with the fertile hydatid cyst, and under the influence of the Pepsin enzyme in the stomach, the protoscolex of the upper part of the small intestine rise in response to the pH change, exposure to bile salts and temperature increase (Thompson and McManus, 2001), where yellow salts in the intestines of the dog help the emergence protoscolex. The protoscolex then communicate deep into the follicles within the Crypts of liberkuhn, and then grow each protoscolex into an adult worm reaching puberty within 6 - 8 weeks depending on the parasite strain and host sensitivity (Lightowlers *et al.*, 2003). Adult worms begin to release eggs or gravid proglottids every 7 to 10 days. Adult worms may remain alive in the final host for 5 - 20 months.

## 6. Structure of Hydatid Cyst

The cyst is made up of the following layers:

### a) Adventitial layer

It is a gelous fibrous layer that surrounds the cyst and consists of the host cells as a result of the host reaction. This layer forms of the glycogen and acts as a barrier to prevent parasite secretions affecting the host's immune system and also inhibits the entry of large macrophages into the sac (Handa *et al.*, 2005).

### b) Lamminated layer

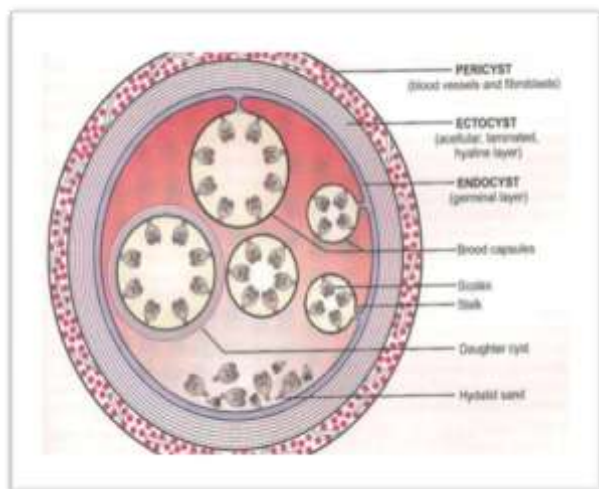
The outer layer of the cyst is characterized by acellular with a coarse rubber composition and white color (Flisser, 2003). This layer is produced

by the parasite, which provides protection from the host's immune responses. This layer consists of a polysaccharide-protein complex. This layer also allows the passage of the immune globulins, but the ability to penetrate the large molecules into the sac is due to the effectiveness. The germinal layer is more than the lamellar layer (Siracusano *et al.*, 2009). The thickness of this layer ranges from about 1 - 2 mm thick and increases its thickness by age and remains strong even after the death of the parasite (Jablawi, 1999).

### c) Germinal layer

The inner lining of the cyst is 20 - 25 microns, consisting of a cellular layer of nuclei that represents the living part of the cyst wall (Schmidt and Roberts, 2000). The germinal layer has several functions, including controlling the permeability of the hydatid cyst and the asexual reproduction, as well as providing protection and attribution to the components of the cyst and the production of the hydatid fluid that fills the cyst cavity (Galindo *et al.*, 2003). The germinal layer is thin and consists of the first two regions called the Tegument region. It is similar in composition to the Tegument wall in the adult worm. Microcirches, which extend towards the Lamminated. The second region is called the cells region, which has several cell types: namely the Tegument cells and muscle cells, glycogen-staining cells and non-differentiated cells (Kang *et al.*, 1992).

Non-differentiated cells proliferate as brood capsules and protoscolex (Gutierrez, 2000). The brood capsules are shaped as small sized lumps that originate from the germinal layer. When the brood capsules containing the protoscolex are separated from the sites associated with the germinal layer, they float in the hydatid fluid, which is known as Hydatid Sand (Rumboldt *et al.*, 2003). The cysts, which are containers on live protoscolex are called Fertile Cysts, while the cysts that does not contain brood capsules or protoscolex are called a sterile cyst (Kamentzk *et al.*, 2000).



**Figure - 1: Hydatid cyst**

## 7. Hydatid fluid

The Hydatid fluid is characterized by a liquid colorless or slightly yellowish fluid that fills the cavity of the cyst. Its specific weight is 1.012 and its pH is between 6.7 - 7.2 and contains a number of enzymes, proteins and salts (Muller and Waklelin, 2001). The hydatid fluid contains protein substances such as albumin, globulin and carbohydrate such as glucose, sucrose, glycogen, and fatty substances such as cholesterol, single and bilateral cholesterol, as well as free and phosphoric lipids, as well as some ions such as sodium, potassium and chloride in addition to a number of enzymes such as Lipase, Protease, Oxidase, Alkaline phosphatase, Glutamic Oxaloacetic Transaminase (GPT). It also contains a group of inorganic elements such as iron, zinc, copper, calcium, magnesium and manganese, as well as bilirubin, ammonia and creatinin, which represent nitrogenous components resulting from the metabolic processes of the parasite (Pedrosa *et al.*, 2000; Radfar and Iranyar, 2004).

## 8. Pathogenicity and Clinical

The incubation period for Cystic hydatidosis varies in humans from several months to years, and can last for 20 - 30 years, especially when the growth of the cyst is slow and undetermined (Craig and Larrien, 2007). Symptoms occur early when the sac is present in specific, Brain, spinal cord, and eyebrow (Gutierrez, 2000). The first stages of the disease are characterized by the absence of any symptoms,

because the size of the cyst in this stage is small, as well as surrounded by capsule from the infected organ (Dvorak *et al.*, 2008). Over time, cyst increase in size and pressure increases on the affected organ. The cyst causes dysfunction of the affected organ, but when the cyst is ruptured and the hydatid fluid is released, it leads to immune reactions, such as urticaria, edema, respiratory symptoms or anaphylactic shock, which may result in death, as well as the release of protoscolex that grow into secondary cysts in different places of the body (Gottsten, 2003; Vuitton, 2004; Eckert and Deplaze, 2004).

The absence of cyst in three areas of the body of the intermediate host is hair, nails and teeth. In the other regions, the cysts can be found in different percentages, which have the highest percentage in the liver and 75 % of the second rank of the lungs and by 20 % and can appear in other parts of the Body by 5 % in both the spleen, kidneys, heart and bones (Paksoy *et al.*, 2005; Fortia *et al.*, 2006). The growth of hydatid cysts in the liver leads to hepatic enlargement of the liver with or without a metatarsal mass during clinical examination in the upper right quadrant, stomach pain in the right side, fever and nausea. The cyst may also compress the bile duct, causing obstructive jaundice, cirrhosis and Cholangitis (Prabhakar *et al.*, 2005; Ezer *et al.*, 2006). In addition, the lung infection causes to put the fluid in the form of sputum. The symptoms are chronic cough, shortness of breath, and pain in the thorax. These symptoms only occur after the size of the cyst becomes large (Brunetti and Filice, 2007). Brain cysts cause head swell and sudden seizures, and brain cysts are often dangerous, lead to headaches, lack of awareness, and severe neurological impairment (Goldman and Bennett, 2000; Schwartz *et al.*, 2008). Cysts that infected bones are abnormal in shape and do not form Lamminated layer. The symptoms are pain in the four limbs, and the cysts in the bones cause gradual erosion of the bone cortex, resulting in osteoporosis (Salinas *et al.*, 2000; Marines *et al.*, 2005). As for the eye, its infection to the cyst is rare and lead to the sharpness of the eyes and lack of visual accuracy and blindness and the

occurrence of an external tumor of the eye (Dandan *et al.*, 2007). The symptoms of this disease are different and depend on several factors including the type of the affected organ, the number, size and condition of the developing cysts, as well as the interaction between the developing cysts and tissue as well as the patient's health status (Kern and Pawlowski, 2002).

## 9. Diagnosis

The diagnosis of Cystic hydatidosis depends on the appearance of disease based on the location and size of the hydatid cyst. There are several ways to diagnose this disease:

### a) Clinical Diagnosis

One of the methods used in the diagnosis of cystic hydatidosis is to rely on epidemiological data and to confirm the presence of the infection in the specific geographical location as well as the appearance of symptoms of the disease on the affected person as a result of the increase in the size of the sac in a particular organ (Gonzalez Sapienez *et al.*, 2000).

### b) Imaging Techniques in Diagnosis

These are multiple techniques that are used depending on the type of organ infected and the phase of the cyst (Polat *et al.*, 2003). Ultrasonography is used to investigate the hydatid cysts in any part of the abdomen or muscles as well as the possibility of elucidating the structure of the cysts in terms of the presence of membranes or barriers and hydatid sand. This method is highly sensitive and is adopted as an initial imaging line, especially in the case of hydatid cyst that has no symptoms (Llica *et al.*, 2007). Computed tomography is used to detect the hydatid cyst in any organ and determine its location, especially for small cysts outside the liver, as well as its ability to differentiate between the infection caused by the hydatid cysts, amoebic infection and purulent cyst (Czermark *et al.*, 2001; Llica *et al.*, 2007). While Magnetic Resonance Imaging (MRI) is used in the examination prior to surgery and in evaluating residual lesions after the procedure (Dursun *et al.*, 2008), lung, bone and abdomen are detected by X-rays and their ability

to detect calcified hydatid cysts (Fortia *et al.*, 2006).

### c) Immunological Diagnosis

One of the most important methods of diagnosis, which depends on the presence of antibodies in the serum of the infected such tests are used to confirm the existence of the infection in some cases of questionable (McManus *et al.*, 2003). These tests include the following: Complement Fixation Test (CFT), Indirect Haemagglutination Test (IHT), Latex Agglutination Test (LAT), Fluorescent Antibody Test (FAT), Immunoelectrophoresis Test (IET) and Enzyme Linked Immunosorbent assay (ELSA).

### d) Molecular Diagnosis

Polymerase Chain Reaction (PCR) is most commonly applied to *Echinococcus multilocularis* eggs through which parasitic DNA was identified (Hashemitabar and Razmi, 2009).

## 10. Treatment methods

The disease of hydatid cyst is very dangerous to human health, so many ways to treat them and depends on a variety of factors, including the size of the cyst and their location and their spread in the body. These methods include:

### a) Surgical Treatment

The best way to treat hydatid cyst is for the possibility of complete removal of the cyst and complete recovery of the patient where the success rate of this method to more than 90 % and the probability of recurrence is very small in rare cases and not dangerous if the location of the cyst is not dangerous and did not develop the disease to advanced stage (Pawlowski *et al.*, 2001; Elissondo *et al.*, 2002), do not prefer surgical method when the presence of multiple cysts in one organ as well as the age of the patient and the pregnancy situation in women and the infection of patients with other diseases such as heart disease and hypertension (Pawlowski *et al.*, 2001; Khuroo, 2002). The risk of surgical interference is the possibility of leakage of the components of the

cyst and thus the spread of the protoscolex and the growth of secondary cyst, which become difficult to remove because of overlapping with different organs of the body (Eckert and Deplozes, 2004). In order to avoid this risk, Albendazole is used for 1 month after surgery. Chemotherapy kills protoscolex and reduces intracranial pressure inside cyst (WHO, 2003; Palanivelu, 2005).

#### **b) Puncture Aspiration Injection Reaspiration**

Puncture Aspiration Injection Reaspiration is one of the most advanced methods of treating Cystic hydatidosis and is used as an alternative method of surgery in the case of cysts that are difficult to remove surgically (Gavidia *et al.*, 2008). This process involves four steps after locating the cyst (Smego *et al.*, 2003).

- Punching of the cyst across the skin by Ultrasonic Guidance.
- Aspiration the components of the hydatid cyst.
- Injection is a lethal substance for the protoscolex such as Formalin, Stromide, Sodium Chloride 20 %, Ethanol 45 % and Alcohol 70 – 95 %). These materials remain in the cyst for 15 minutes.
- Reaspiration the components of the cyst again.

#### **c) Pharmacological Treatment**

That the failure of surgical operations completely was one of the reasons that prompted the researchers to use chemotherapy, as well as some cases that hinder the operation of surgery as age and pregnancy, as well as cysts located in locations difficult to carry out the operation (Pawlowski *et al.*, 2001). Benzimidazole derivatives are the most commonly used drugs, which have been effective in killing protoscolex, such as Albendazole, Mebendazole and others (Reuter *et al.*, 2006).

#### **d) Immunological Treatment**

Immunomodulators, which are substances that alter and increase the efficiency of the immune system. A number of researchers have conducted studies on these substances for the treatment of Cystic hydatidosis (Weir, 1992). The

BCG vaccine and the Polycyclic Stearate (L.P.S), Hormone estrogen and Progesterone, as well as the toxic parts of the hydatid cyst. One of the most important substances used in immune modification, studies have shown the ability of these substances to raise the immune response as well as the ability of the material to reduce the weights and numbers and diaries of secondary hydatid cyst (Al-Taei, 1996).

#### **e) Radiotherapy**

Several experiments have been conducted on the possibility of using radiation to inhibit the growth of neural bags, and the types of radiation used are: X-ray, Y-ray, Laser Ray and Ultra Violet Rays (Movesijan *et al.*, 1968; Mosimann, 1980; Al-Masudi, 1989).

#### **f) Medical Plants Therapy**

Throughout the world, humans have been using medicinal plants to treat many diseases without relying on industrially prepared compounds. The Babylonians, Assyrians, and Sumerians were described in Iraq as the first pharmaceutical record, containing about 150 pharmaceutical, plant and animal preparations, and manufactured pharmaceuticals such as suppositories. Recently, attention has been paid to the use of plant extracts in the treatment of several diseases affecting humans, including Cystic hydatidosis, where they may find a cure for this disease (Kang, 1994). Perhaps the most prominent reasons for the increased interest in medicinal plants containing the components of effective used as anti-disease due to the resistance of pathogens to many antibiotics, medicinal plants contain inert constituents that have no medical or functional effect, such as cellulose, lactin and suberin, as well as active constituents that include volatile oils, glycosides, saphones, tannins, alkaloid, lipids, carbohydrates, Resines and sterols (Oran and Raies, 2000). One of the plant extracts used in the treatment of hydatid cysts, extract of *Perganum harmala*, *Cyperus rotundus*, *Allum sativum*, *Artemisia herba-alba*, *Achillea micrantha*, *Eucalyptus*, *Myrtus communis*, *Apium graveolens*, *Trigonella foenum*, *Nigella sativa*,

*Citrullis colocyntis*, *Thymus spicata* etc. (Anah, 2012).

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**DOI Number**

[DOI: 10.22192/lisa.2020.6.6.3](https://doi.org/10.22192/lisa.2020.6.6.3)

**Thomson Reuters Researcher ID**

L – 5547 – 2016

**ISI Impact Factor**

4.206

**How to Cite this Article:**

**Saad Aziz Anah, Ennas Mohamad Majhwol, Haifaa M. Jawad and Sadiya A. Anah. 2020. Human Echinococcosis: A Review. *Life Science Archives*, 6(6): 1996 – 2008.**

[DOI: 10.22192/lisa.2020.6.6.3](https://doi.org/10.22192/lisa.2020.6.6.3)