Journal of Natural Sciences Research www.iiste.org
ISSN 2224-3186 (Paper) ISSN 2225-0921 (Online)
Vol.5, No.14, 2015

The Possible Role of Different Experimental Doses of Cadmium in the Damage of Architecture of Mice Kidney

Ahmed Anwar Albir
Department of Basic Sciences, College of Dentistry, University of Baghdad, Baghdad, Iraq

Abstract:
In the present investigation, 18 healthy male Swiss albino mice (weighing 30-35g) served as experimental material were divided into three groups.Each group consisting six mice. Group I was only given tap water as control during experimentation period (36 days), group II and group III were daily given a subcutaneous injection of cadmium in the form of cadmium chloride ($CdCl_2$) at a dose of 3mg and 6mg/Kg body weight respectively. Sections of kidneys were prepared and examined by light microscope. Histopathologicalobservations revealed marked degeneration in the architecture of the renal cortical structures (glomeruli and tubular cells) of the experimental groups (group II and group III) of mice respectively when compared to healthy control group.
Keywords: cadmium, histopathology, mice

1. Introduction:

Cadmium is one of the most important toxic metals due to its accumulation in the environment as a result of its industrial, agricultural use and tobacco smoking(Godt*et al*. 2006). It has been reported that cadmium may cause injury of various tissues in humans and animals (Godt*et al*. 2006). Among many toxic effects, this pollutant is known to cause sterility (Bench *et al*. 1999), renal dysfunction(Cai*et al*. 2001), liver and pancreas damage (Horiguchi *et al*. 2000, Shimada *et al*. 2000). Additionally, cadmium exerts genotoxic and apoptotic effects (Fahmy&Aly 2000, Kim *et al*. 2005), modulates synaptic neurotransmission (Minami *et al*. 2001) and induces changes in the brain antioxidant status (Carageorgiou*et al*. 2004).

Studies on animals have shown that Cd is a stimulator for formation of reactive oxygen species (ROS) (Amoruso& Goldstein 1982), hydrogen peroxide (Wong *et al*. 1990), and also hydroxyl radicals (Ochi *et al*. 1998). These free radicals enhance lipid peroxidation, DNA damage, altered calcium and sulfhydryl homeostasis (Sugiyama 1994, Lonard*et al*. 2004, Valko*et al*. 2005). These free radicals also affect cellular function by perturbing signal transduction, such as protein kinase C (PKC), mutagen activated protein kinase (MAPK), and cyclic AMP pathway; however, the mechanism is largely unknown (Joseph *et al*. 2001, Lag *et al*. 2005).

Lipid peroxidation is the primary mechanism for Cd-induced toxicity (Enemane*t al*. 2000). Through the Fenton reaction, oxidative stress produces hydroxyl radical species that are believed to initiate lipid peroxidation (Murugavel&Pari 2010, Yiin*et al*. 1999). Following this process, free radicals are produced and attached to any available molecule in intracellular environment or the extra one which eventually leads to cellular damage (Murugavel&Pari 2010, Yiin*et al*. 1999). Therefore, the present investigation was designed to evaluate kidney damage induced by cadmium, which is related to the oxidative damage in the architecture of mice kidney.

2. Materials & Methods

In the present investigation, 18 healthy male Swiss albino mice (weighing 30-35g) served as experimented material, were divided into three groups. Each group consisting six mice. All animals were handled under standard laboratory conditions of a 12h light/ 12h dark cycle in a temperature and humidity controlled room. A standard chow diet and water were available free access. The first group was only given tap water as control during experimentation period (36 days). Group II and group III of mice were daily given a subcutaneous injection of cadmium in the form of cadmium chloride ($CdCl_2$) at a dose of 3 mg and 6mg/ Kg body weight respectively.

Twenty-four hours after latest injection, two animals from both control and the experimental groups were anaesthetized by chloroform and their kidneys were rapidly obtained and fixed in 10% formalin (the other four mice from each group were kept upon need). The kidneys were dehydrated in alcohol, then placed in xylene to remove alcohol and embedded in paraffin wax. The embedded kidneys in paraffin were sectioned by a microtome. The sections were stained by using hematoxylin and eosin procedure. A drop of Canada balsam was placed on each section and covered with a cover slip and allowed to dry. The sections were prepared for histopathological investigation by light microscope.

3. Statistical Analysis

By using non-parametric test, such as K.S. (Kolmogorov-Smirnov) test, there was a significant correlation between the given experimental dose and the degenerative changes that occurred in the kidney structure, $P<0.05$.

4. Results

4.1Group I: Control group

Was only given tap water during experimentation period (36 days). The examination of the histological sections of the control kidneys of mice show normal architecture (Figure 1). The cortex is mostly occupied by renal corpuscles and surrounding proximal and distal convoluted tubules. The renal corpuscle is formed of glomerular tuft of blood capillaries surrounded by capsular space and Bowman's capsule.

4.2 Group II

Was daily given a subcutaneous injection of cadmium in the form of cadmium chloride ($CdCl_2$) at a dose of 3mg/Kg body weight.

The examination of the histological sections showed the following obvious histological changes in the architecture of mice kidney (Figure 2) when compared to normal histoarchitecture of mice kidney (control group):

- Congested glomeruli.
- Diminution of both epithelium and lumen of the renal cortical tubules (proximal and distal convoluted tubules), and collecting duct.

4.3 Group III

Was daily given a subcutaneous injection of cadmium in the form of cadmium chloride ($CdCl_2$) at a dose of 6 mg/Kg body weigh.

The examination of the histological sections showed the following severe degenerations in the histoarchitecture of mice kidney (Figure 3) when compared to group II mice kidney:

- Swelling of the entire renal corpuscle and destruction of the kidney glomerulus with disappearance of its epithelium were detected.
- Swelling of the renal cortical tubules that can hardly be distinguished with presence of vacuoles in the cytoplasm and dark appearance of the nuclei of the tubular cells.

5. Discussion

Renal damage caused by certain toxic chemical materials considered as public health problem (Sharma *et al*. 2012). Damage due to oxidation takes place in the tissue when the given dose exceeds the antioxidant capacity of the tissue (Gupta & Sharma 2011). The nephrotoxicity has a great concern because the kidneys are the major targets of the excretion of the drug. However, the nephrotoxicity causes cell death finally so it is necessary to define the mechanism in addition to the site of action, to lead us to exact steps that must be done for avoidance of damage occurrence (Sharma &Janmeda 2013). The molecular mechanism for describing the toxic effect of cadmium is not well-understood, but it is obvious that Cd itself is unable to generate damage and it has been shown that the relationship between Cd and free radicals is indirect (Murugavel&Pari 2010). During carcinogenesis, the free radicals caused damage to the membrane and cytosolic components which protected by antioxidants (Banakar*et al*. 2004, Singh &Pracheta 2012). The antioxidants protect membrane and cytosolic components against damage caused by free radicals during carcinogenesis (Banakar*et al*. 2004, Singh &Pracheta 2012). Thus, antioxidants are supposed to decrease the liability of the kidney to be damaged to oxidative challenges (Rodrigo & Rivera 2002).

Our experimental present work was undertaken to prove and provide sufficient evidence that remarkable damage was occurred in the histoarchitecture of the mice kidney injected with cadmium in the form of cadmium chloride ($CdCl_2$) at particular doses (both second and third experimental groups of mice were daily given a subcutaneous injection at a dose of 3mg and 6mg/Kg body weight respectively) during experimentation period (36 days). The examination of the histological sections of mice kidney of the third experimental group showed more severe damages especially in the histoarchitecture of kidney glomerulus when compared to the degenerated structure of mice kidney of the second experimental group (congested glomeruli and diminution of both epithelium and lumen of the renal cortical tubules and collecting duct) such as swelling of the entire renal corpuscle and destruction of the kidney glomerulus with disappearance of its epithelium, and swelling of the renal cortical tubules (hardly be distinguished) with cytoplasmic vacuolation and dark appearance of the nuclei of tubular cells which can be explained by suppression of the antioxidant defense systems caused by the increase in the dose of cadmium. Our work can be considered as subchronic study.

The overall results arising from our present experimental work are not consistent with what reported previously (Thijssen*et al*. 2007) that a chronic exposure to low Cd concentrations triggered a biphasicdefence activation in the kidney that might lead to adaptation and survival. However, some of our results are in agreement with those also reported previously (Brzoska*et al*. 2003, Piscator 1986, Thijssen*et al*. 2007) that chronic exposure to cadmium compounds can damage the renal proximal tubular epithelial cells (except of the experimentation period of our subchronic investigation).

Our results in this experimental work showed that Cd has ability in accumulation in kidneys cells and could harmful for nucleus and the cytoplasm (little information has been published about the damage that could be occurred in the architecture of tubular cells of the cortex of the kidney induced by cadmium). Therefore we suggest that individuals who are exposed to cadmium must improve their antioxidant defense system by continual medical consultation.

6. Conclusion

It could be concluded that at particular gradual doses of cadmium during experimentation period, cadmium has the ability to damage the normal histoarchitecture of kidney glomerulus and other renal cortical structures such as tubular cells severely.

Last but not least, also the results of our experimental work may encourage the researchers in the future to do further studies in order to promote our knowledge about the dangerous effects of cadmium on the human life and environment experimentally.

References

Amoruso,M.A. &Goldstein, B.D. (1982), "Enhancement of rat and human phagocyte superoxide anion radical production by cadmium in vitro",*Toxicology Letter*10, 133-8.

Banakar, M., Paramasivan, S.K., Chattopadhyay, M.B., Datta, S., Chakraborty, P. &Chatterjee, M.*et al.* (2004),"1 alpha, 25-dihydroxyvitamin D3 prevents DNA damage and restores antioxidant enzymes in rat hepatocarcinogenesis induced by diethylnitrosamine and promoted by phenobarbital",*World J Gastroenterol*10, 1268-75.

Bench, G., Corzett, M. H., Martinelli, R.&Balhom, R. (1999),"Cadmium concentrations in the testes, sperm, and spermatids of mice subjected to long-term cadmium chloride exposure",*Cytometry*35, 30-6.

Brzoska,M.M., Kaminski,M.,Supernak-Bobko, D.,Zwierz,K.&Moniuszko-Jakoniuk, J. Changes in the structure and function of the kidney of rat chronically exposed to cadmium. Archive of Toxicology.2003, 77 (Biochemical and histopathological studies).

Cai, Y., Aoshima, K., Katoh, T., Teranishi, H.&Kasuya, M. (2001), "Rebal tubular dysfunction in male inhabitants of a cadmium-polluted area in Toyama, Japan-an eleven-year follow-up study",*J Epidemiol*11, 180-9.

Carageorgiou, H., Tzotzes, V., Pantos, C., Mourouzis, C., Zarros, A.&Tsakiris S. (2004), "In vivo and in vitro effects of cadmium on adult rat brain total antioxidant status, acetylcholinesterase (Na+, K+)-ATPase and Mg^{2+} ATPase activities: protection by L-cisteine", *Basic ClinPharmacolToxicol*94, 112-8.

Eneman, J.D., Potts, R.J.,Osier,M.,Shukla,G.S.,Lee,C.H. &Chin, J.F. (2000), "Suppressed oxidant induced apoptosis in cadmium adapted alveolar epithelial cells and its potential involvement in cadmium carcinogenesis", *Toxicology*7, 215-28.

Fahmy,M.A.&Aly, F.A. (2000), "In vivo and in vitro studies on the genotoxicity of cadmium chloride in mice",*J ApplToxicol*20, 231-8.

Godt, J., Scheidig, F., Grosse-Siestrup, C., Esche, V., Branderburg, P.& Reich, A, *et al.*(2006), "The toxicity of cadmium and resulting hazards for human health",*J Occup Med Toxicol*1,22.

Gupta, R.& Sharma, V. (2011), "Ameliorative effects of tinosporacordifolia root extract on histopathological and biochemical changes induced by aflatoxin-b(1) in mice kidney",*ToxicolInt*18, 94-8.

Horiguchi, H., Harada, A., Oguma, E., Sato, M., Homma, Y.&Kazama, F, *et al.*(2000), "Cadmium-induced acute hepatic injury is exacerbated in human interleukin-8 transgenic mice",*ToxicolApplPharmacol*163, 231-9.

Joseph,P.,Muchnok,T.K.,Klishis,M.L., Roberts,J.R.,Antonini, J.M.&Whong,W.Z.,*et al.*(2001), "Cadmium-induced cell transformation and tumorgenesis are associated with transcriptional activation of c-fos, c-jun, and c-mey proto-onchogenes", *Toxicology Science*61, 295-303.

Kim, S.D., Moon, C. K., Eun, S.Y.&Ryu, S.A Jo.(2005), "Identification of ASK1, MKK4, JNK, c-Jun, and caspase-3 as a signaling cascade involved in cadmium-induced neuronal cell apoptosis",*BiochemBiophys Res Comm*328, 326-34.

Lag, M.,Refsnes,M.,Lilleaas,E.M.,Holme,J.A.,Becher,R.&Schwarze,P.E. (2005),"Role of mitogen activated protein kinases and protein kinase C in cadmium-induced apoptosis of primary epithelial lung cell",*Toxicology*211, 253-64.

Leonard, S.S., Harris, G.K.&Shi, X. (2004), "Metal-induced oxidative stress and signal transduction",*Free Radical Biology and Medicine*37, 1921-42.

Minami, A., Takeda, A., Nishibaba, D., Takefuta, S.& Oku, N. (2001), "Cadmium toxicity in synaptic neurotransmission in the brain",*Brain Res*894, 336-9.

Murugavel, P.&Pari.L.(2010), "Effect of diallytetrasulfide on cadmium-induced oxidative damage in the liver of rats", *Human Experimental Toxicology*26, 527-34.

Ochi,T.,Otsuka, F., Takahashi,K.&Oshawa, M. (1998), "Glutathione and metallothioneins as cellular defense against cadmium toxicity in culture Chinese hamster cells", *Chemistry and biology interaction*65,1-14.

Piscator, M. (1986), "The nephropathy of chronic cadmium poisoning. In: E.C. Foulkes, editor",*Handbook of experimental pharmacology*New York, Springer, 180-94.

Rodrigo, R.& Rivera, G. (2002), "Renal damage mediated by oxidative stress: A hypothesis of protective effects of red wine",*Free RadicBiol Med*33, 409-22.

Sharma, V.&Janmeda, P. (2013), "Chemopreventive role of Euphorbia neriifolia (linn) and its isolated flavonoid against n-nitrosodiethylamine-induced renal histopathological damage in male mice",*ToxicolInt*20(1), 101-107.

Sharma, V., Janmeda, P.& Singh L. (2012), " N-Nitrosodiethylamine and carcinogenicity: An Over review",*Int J Environ RehabilConserv*3, 56-67.

Shimada, H., Funakoshi, T.&Waalkes, M.P. (2000),"Acute nontoxic cadmium exposure inhibits pancreatic protease activities in the mouse", *ToxicolSci*53, 474-80.

Singh, L.&Pracheta.(2012), "Cancer: Plant Based Chemoprevention and Therapy: An Overview", *J Biochem Cell Arch*12, 1-20.

Sugiyama, M. (1994), "Role of cellular antioxidants in metal-induced damage",*Cell Biology andToxicology*10, 1-22.

Thijssen,S.,Cuvpers,A.,Maringwa,J.,Smeets,K.,Horemans,N.,Lambrichts, I.&Van Kerkhove, E. (2007), "Low cadmium exposure triggers a biphasic oxidative stress response in mice kidneys",*Toxicology*236(1-2), 29-41.

Thijssen, S.,Maringwa,J.,Faes,C.,Lambrichts,I.&van Kerkhove, E. (2007), " Chronic exposure of mice to environmentally revalent, Low doses of cadmium leads to early damage, not predicted by blood or urine cadmium levels", *Toxicology*299, 145-56.

Valko,M., Morris,H.&Cronin, M.T. (2005),"Metals, toxicity and oxidative stress",*Current Medicinal Chemistry*12, 1161-208.

Wong, Z., Troll,W.,Koenig, K.L.&Frenkel, K. (1990), "Carcinogenic sulfide salts of nickel and cadmium induce H_2O_2 formation by human polymorphonuclear leukocytes", *Cancer Research*20, 7564-70.

Yiin, S.J.,Chern,C.L.&Shen, J.Y. (1999), "Cadmium-induced renal lipid peroxidation in rats and protection by selenium".*Journal of Toxicology and Environmental Health*57, 403-13.

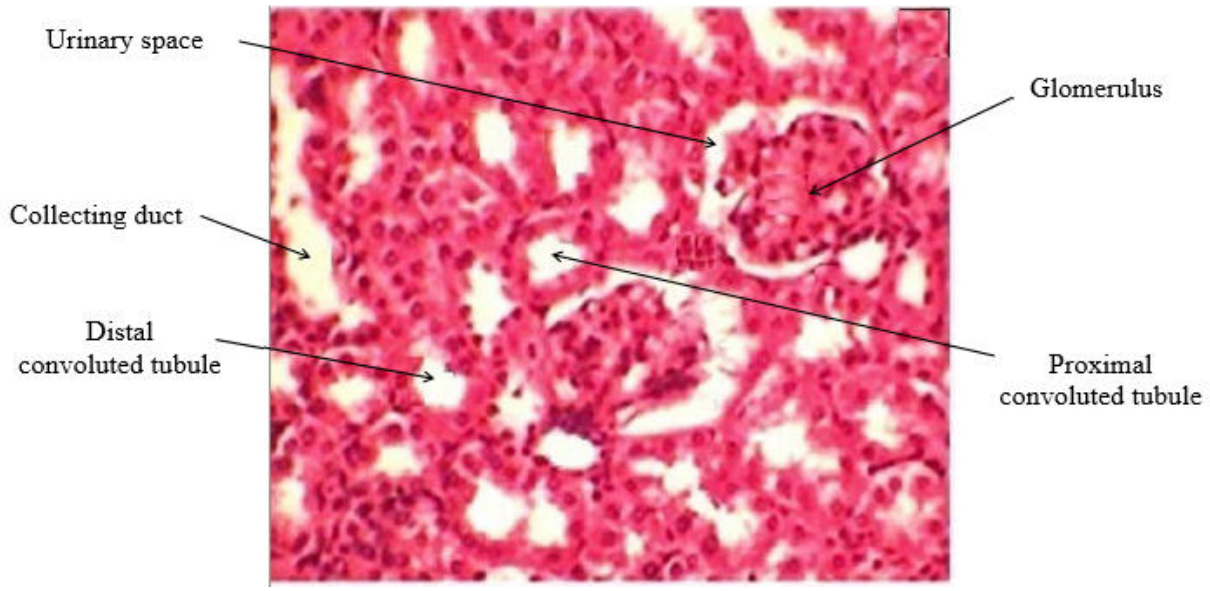

Figure 1. Section of deep cortical area of mice kidney (control group) showing normal histoarchitecture of the kidney cortex. Stain: Hematoxylin and Eosin, X40.

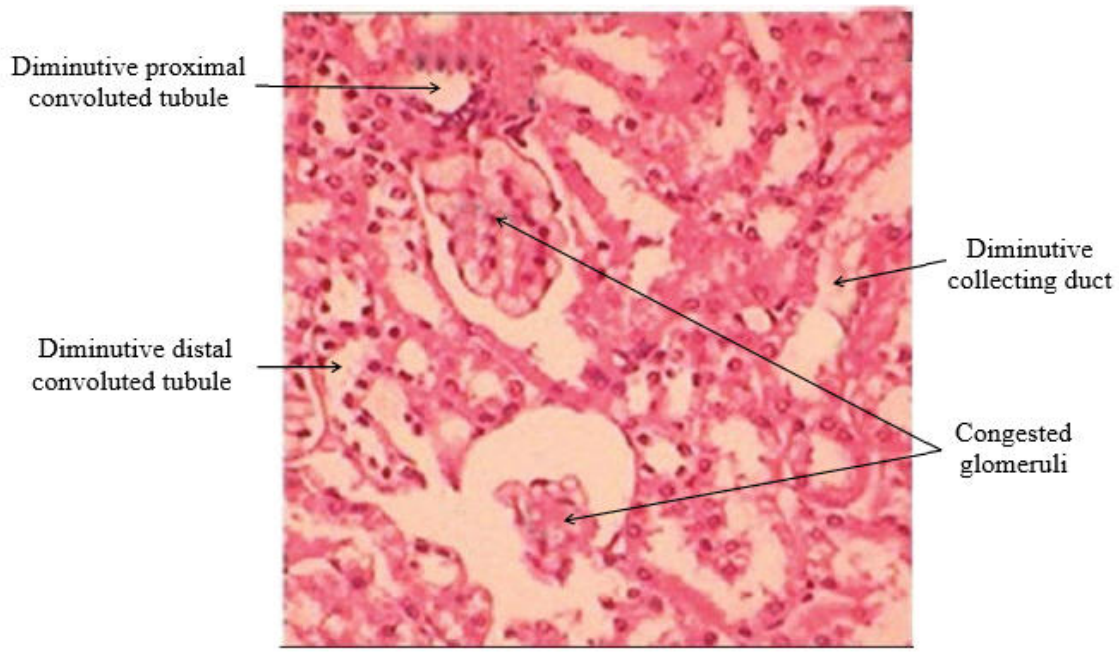

Figure 2.Section of deep cortical area of mice kidney of second experimental group.Stain: Hematoxylin and Eosin, X40.

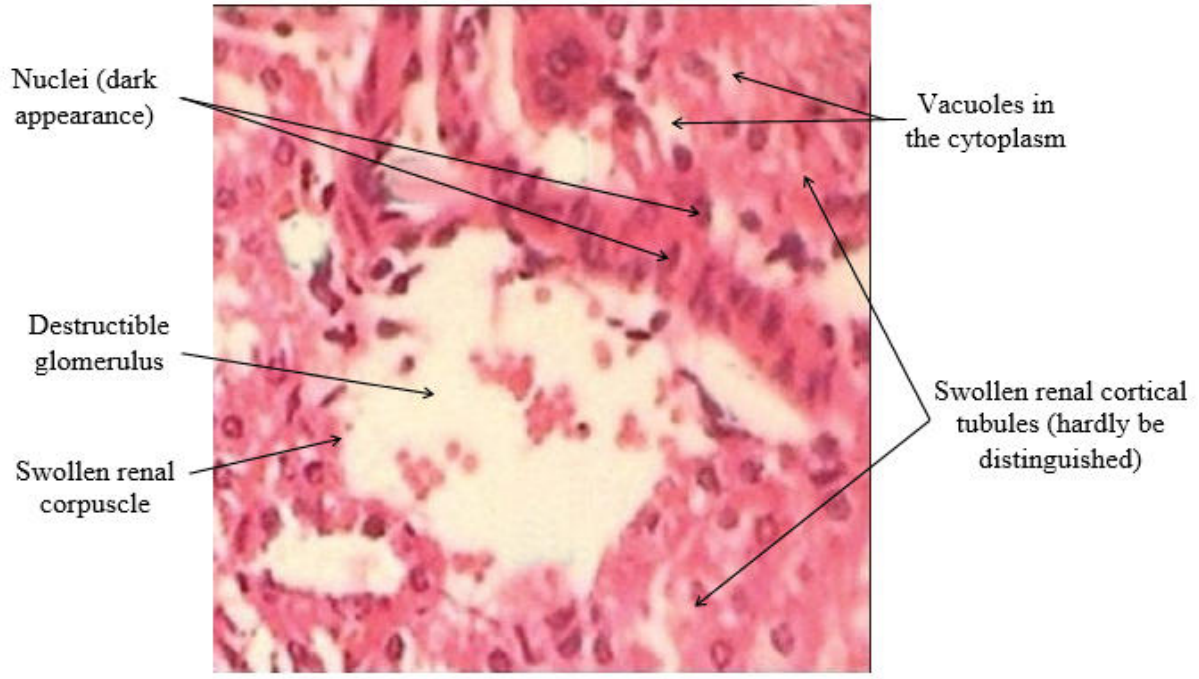

Figure 3.Section of deep cortical area of mice kidney of third experimental group.Stain: Hematoxylin and Eosin, X40.

The IISTE is a pioneer in the Open-Access hosting service and academic event management. The aim of the firm is Accelerating Global Knowledge Sharing.

More information about the firm can be found on the homepage:
http://www.iiste.org

CALL FOR JOURNAL PAPERS

There are more than 30 peer-reviewed academic journals hosted under the hosting platform.

Prospective authors of journals can find the submission instruction on the following page: http://www.iiste.org/journals/ All the journals articles are available online to the readers all over the world without financial, legal, or technical barriers other than those inseparable from gaining access to the internet itself. Paper version of the journals is also available upon request of readers and authors.

MORE RESOURCES

Book publication information: http://www.iiste.org/book/

Academic conference: http://www.iiste.org/conference/upcoming-conferences-call-for-paper/

IISTE Knowledge Sharing Partners

EBSCO, Index Copernicus, Ulrich's Periodicals Directory, JournalTOCS, PKP Open Archives Harvester, Bielefeld Academic Search Engine, Elektronische Zeitschriftenbibliothek EZB, Open J-Gate, OCLC WorldCat, Universe Digtial Library , NewJour, Google Scholar