

Effect of Source of Silica on Properties of Fe₂O₃/SiO₂ Nanocompsites and Their Application on Hepatic Injury in Rats as Adsorbents for Removal of Heavy Metal from Drinking Water

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Received: 25 September 2017;	Accepted: 12 December 2017;	Published online: 31 January 2018;	AJC-18756
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A series of iron oxide silica composites (70/30, 50/50 and 30/70) were prepared using rice hull silica gel as natural silica and TEOS. The prepared samples were characterized by X-ray diffraction, FTIR spectra, BET measurement and SEM. The results show that the particle size is dependent synthesis conditions. BET measurement showed that the values of surface area of the samples are on the range of (320-43 m²/g) and increase with increasing the iron content. The results showed that the surface area of composites prepared from nature silica is lower than that prepared from TEOS. This result was explained on the basis of particle size effect. SEM showed that the size and homogeneity of particles are independent on the Fe₂O₃ content. Additionally, the effect of drinking water heavy metals (DWHM: Pb, Hg, Ni, Fe and Mg) and DWHM purified with nature silica and TEOS (0.05 and 1.0 g/L.W) on liver injury was evaluated in male rats, as manifested by changes in the activities of certain serum enzymes, such as Fasting blood sugar (FBS), TC, LDL-C, HDL-C, TG, ALT and AST were determined as markers of liver disease. In addition, ALP, γ -glutamyltransferase (GGT), LDH and CK were also determined in male rats. The results showed significantly (p \leq 0.05) deceased in serum TC, TG, LDL, AST, ALT, ALP, FBS and LDH in male rats administration of DWHM purified with nature silica and TEOS (0.05 and 1.0 g/L.W) compared to rats administration of DWHM (PC). On the other hand, HDL and CK were increased significantly (p \leq 0.05) compared to PC. All these results were accompanied by histological observations in liver. The results demonstrate that nature silica has a beneficial effect in DWHM purification than TEOS.

Keywords: Fe₂O₃/SiO₂, Nanocomposites, Drinking water, Heavy metals, Hepatic injury, Nature silica.

INTRODUCTION

Water contamination with heavy metals has become the prime focus of environmental scientists because it is one of the clear signs of prosperity, health, serenity, beauty, artistry, purity and many other attributes [1]. Heavy metal in water could be derived from both natural (weathering and erosion of bed rocks and ore deposits) and anthropogenic (mining, industries, wastewater irrigation and agriculture activities) sources [2-4]. It may contaminate the surface water and groundwater resulting in deterioration of drinking and irrigation water quality [5] and considered as severe pollutants owing to their toxicity, persistence and bioaccumulative nature in environment [6]. High concentrations of manganese and lead are considered highly toxic for human and aquatic life [7]. Lead is a highly toxic and carcinogenic metal and may cause chronic health risks, including headache, irritability, abdominal pain, nerve damages, kidney damage, blood pressure, lungs cancer, stomach cancer and gliomas [8-10]. Also, manganese in drinking water can cause mental diseases such as Alzheimer's and

Manganism [11]. As the same, the nickel sulfate and nickel chloride ingestion can cause severe health problems, including fatal cardiac arrest [12]. Several studies have investigated a range of innovative techniques for the efficient removal of contaminants from polluted water. Remediation techniques for water treatment can be categorized into biological, chemical and physical treatment methods [1]. The adsorption of contaminants is broadly used due to the simplicity and economics of this approach. The removal efficiency by adsorption is mostly determined by the properties of an adsorbent and several materials have been used as adsorbents, such as activated carbons [13,14], zeolites [15,16], iron oxides [17,18] and silica [19].

Rice hull is a good source of lignin, cellulose, hemicellulose and silica [20,21], also used as a source of microbial nutrients for production single-cell protein [22] and reducing sugar and as a raw product for ethanol and furfural manufacturing [23,24]. The rice industry has optimized a technology to burn rice hull as an energy source and produce rice hull ash (RHs) which has $\approx 60 \%$ silica. Some researchers were used chemical process to produce silica gel from rice hull silica and is widely used in a range of cosmetics, pharmaceutical and paint [25,26]. Rice hull silica is amorphous and is ≈ 20 % of the rice hull. While, the ash from the unwashed hull contains about 96 % (w/w) silica and some amount of organics, alkali oxide and impurities but with an appropriate washing of the hull, the ash can contain > 99 % (w/w) silica [27]. The silica in rice hull is transforms from amorphous to crystalline silica when it is heated at high temperatures. The transformation temperature is affected by its chemical purity and particle size. Mohamed *et al.* [28] reported that silica derived from rice husk an undesirable agricultural mass residue that contains metal ion impurities such as TiO₂ and Fe₂O₃ is chemically treated with NaOH to prepare amorphous silica [29].

Nanostructured materials have been the subject of intense research lately because of unusual physical properties exhibited by them and their potential applications. The synthesis of nanodots, nanowires, nanobelts, etc. of different materials has posed challenging tasks to materials scientists. Mostly physical and chemical methods have been used to grow nanomaterials in different forms [29]. Silicate glass structure has substantial amount of void space within it. Nanometer sized particles can be accommodated in these glasses. The sol-gel reaction has become one important technique to prepare high-performance materials [30]. Consequently nanomaterials may be harmful to the biosphere although original substances cause no toxicity. Thus, the facile separation of nanosturctured sorbents is very important in their industrial applications in order not to make a harmful impact to the environment. SiO₂-supported Fe₂O₃ materials have been extensively used as sorbent for a wide variety of reactions because their physicochemical properties are superior to those of the single oxides [31]. The properties of the Fe₂O₃/SiO₂ systems depend on the synthesis conditions and on the degree of interaction between the two oxides. Therefore, in this article, we reported the preparation and characterization of magnetite-silica nanocomposites, in which silica was obtained from rice hull as natural silica gel and from $Si(C_2H_5)_4$. The efficiency of natural silica and TEOS composition as adsorbents for removal heavy metals from drinking water and to Study the effect of DWHM and DWHM purified with natural silica and TEOS on liver injury in male rats.

EXPERIMENTAL

A series of iron oxide silica composites were prepared by mixing an alcoholic solution of TEOS (Fluka) and aqueous solution of iron chloride (FeCl₃·6H₂O, Fluka) using a small amount of HCl in water and ethyl alcohol [32]. Natural silica was extracted from rice hulls by boiling rice hulls with NaOH (1 M) in a covered Erlenmeyer flask for 1 h with constant stirring. The solution was filtered through Whatman No. 3 filter paper [33]. Sol-gel method was carried out under high acidic conditions at pH<2 in order to prevent precipitation of iron hydroxide. After gelation at room temperature, the obtained xerogels were dried at 100 °C. Then the dried xerogels were fired at 900 °C for 1 h. The SiO₂/Fe₂O₃ ratio was (70:30) sample A2, (50:50) sample B2 and (30:70) sample C2.

Characterization: X-ray diffraction was carried using Diano Corporation USA diffractometer with a monochromated Co radiation ($\lambda = 0.179$ nm). Surface morphology was inves-

tigated by SEM (Jeol JXA-840 electron probe microanalyzer). The BET surface area and mean pore radius (r) were determined from N_2 adsorption isotherm using conventional or classical volumetric apparatus. The chemical species and the chemical bonding state at different processing parameters were studied employing FTIR spectroscopy (Nicolet spectrometer model 670 FT-IR) in the wave number range 4000-400 cm⁻¹ using KBr pellet.

Animals and experimental design: Eight week old male Wistar rats weighing 180-200 g were used. The animals were kept at constant room temperature (25 °C) with 12 h of light/ dark cycles. All animals received normal rat chow and had access to distilled water *ad libitum* during the acclimatization period. The individual animal body weight was recorded weekly throughout the experiment. All together, we had six groups comprising of four groups each for Mn, Hg, Fe, Ni and Pb, the other groups include the control (positive and negative control).

Preparation of nutrient substance and heavy metals: The preparation and composition of diet was done as reported [34]. Exposed groups received distilled water that contained 100 ppm lead acetate, 1000 ppm manganese chloride, 100 ppm nickel chloride, 1200 ppm iron chloride and 10 ppm mercury chloride. The percentage (%) mixture was mirrored to the recommended daily dose for this nutrient substance [35].

Experimental protocol: Group 1 was fed normal rat chow and either one (group 2) of the heavy metals (Mn = 1000 ppm; Hg = 10 ppm; Pb = 100 ppm, Ni = 100 ppm, Fe = 1200ppm) in drinking water (DWHM). Group 3 and 4 were fed rat chow natural silica at 900 °C (0.05 and 1.0 g/L.W (Water)) + DWHM, Group 5 and 6 were fed rat chow TEOS at 900 °C (0.05 and 1.0 g/L.W) + DWHM. All administrations were through the oral route. Total feed consumption was weighted, fresh feed was provided every day and total body weight of the animals was recorded at the beginning and during the experimental period. Blood samples were collected from the orbital plexus by mean of heparinized capillary glass tubes according [36]. Each sample was placed into a dry clean centrifuge tube and centrifuged 1500× g for 30 min at 4 °C to obtain serum.

Biochemical assays

TC, **TG**, **HDL**, **LDL**, **ALT** and **AST** assays: Total cholesterol (TC) was determined according to the method described by Allain *et al.* [37]. TG was determined according to the method described by Fossati and Prencipe [38]. HDL-C was determined according to the method described by Lopez-Virella *et al.* [39] and LDL-C was determined according to the method described by Friedewald *et al.* [40]. Serum transaminases sAST and sALT (aspartate transferase and alanine transferase) were measured colorimetrically according to the method described by Reitaman and Frankel [41].

Determination of fasting blood sugar (FBS): Fasting blood sugar of the rats was measured at intervals using a glucometer with strips (Prestige IQ ® blood monitoring system, AR-Med LTD, Runny Mede Malthouse, Egham TW209BD, UK). A drop of blood is placed on the strip and the appropriate blood sugar concentration is displayed on the glucometer screen after 10-50 s. The glucometer employs glucose oxidase principle for blood glucose measurement [42]. **ALP and LDH assays:** Serum alkaline phosphatase (ALP) and lactate dehydrogenase activities (LDH) were determined according to Bablok [43].

\gamma-GT and CK assays: Serum γ -GT and CK were determined according to Tietz [44].

Histopathological examination: For microscopic evaluation, livers were fixed in 10 % neutral phosphate buffered formalin solution. Following dehydration in an ascending series of ethanol (70, 80, 90, 100 %), tissue samples were cleared in xylene and embedded in paraffin. Tissue sections of 5 μ m were stained with hematoxy-lineosin (H-E). A minimum of 10 fields for each liver slide were examined and assigned for severity of changes by an observer blinded to the treatments of the animals.

Statistical analysis: Results were expressed as mean SEM. The intergroup variation was measured by one way analysis of variance (ANOVA) followed by Fischer's LSD test. Statistical significance was considered at ($p \le 0.05$). The statistical analysis was done using Jandel Sigma Stat Statistical Software version 2.0.

RESULTS AND DISCUSSION

Characterization of Fe₂O₃/SiO₂ composites: X-ray pattern of iron oxide silica composites shows that γ -Fe₂O₃ phase appears in all samples [45] (Fig. 1a-c).



Fig. 1. X-ray diffraction patterns of iron oxide silica composites, C2 (a), B2 (b), A2 (c) and nature silica (d)

X-ray was also used to determine particle size using equation [32]:

$$d = \frac{0.94\lambda}{\beta\cos\theta}$$

where d average crystallite size, λ the X-ray wavelength, θ the diffraction angle, β the full width at half maximum (FWHM).

The determined size of 70/30, 50/50 and 30/70 silica iron oxide composites was 36.2, 115 and 3.5 nm, respectively. This was derived from FWHM at $2\theta = 22.1^{\circ}$. This shows that particle size is dependent synthesis conditions. This indicates that the smallest particle size was obtained for composites 30/70. So that, this composite was selected to prepare from natural silica.

Fig. 1d shows the X-ray for nanocomposite prepared from natural silica. It is noticed that 30/70 nanocomposite is in γ -Fe₂O₃ crystalline phase. This means that change source of silica don't affect on its crystal structure.

Fig. 2 shows the IR spectra of Fe_2O_3 silica nanocomposites powder. As shown in these spectra, the broad band at 3435 cm⁻¹ is ascribed to the stretching modes and H-O-H bending vibration of the free or absorbed water. Strong absorptions at 1098, 791, 465 cm⁻¹ indicate the formation of silica network [32]. No characteristic bands of Fe-O-Si bonds are appeared in the spectra, which indicates that there is no interaction between Fe₂O₃ and silica matrix [46]. The peak situated at 960 cm⁻¹ is due to Si-OH stretching of silanol terminal groups disappears, indicating the progress of the polycondensation process as a consequence of thermal treatment [47]. Also, the band at 1098 cm⁻¹ for Si-O-Si of SiO₄ tetrahedron and the band at 465 cm⁻¹

Fig. 3 shows the IR spectra of Fe_2O_3/SiO_2 nanocomposite powder prepared from natural silica with composition 30/70. It is also noticed that changing nature of silica does not affect the characteristic band of silica.

Nitrogen adsorption/desorption isotherms for all composites are shown in Fig. 4. All the analyzed iron-silica particles share the type of isotherm, corresponding to type I which characteristic of microporous materials. Fig. 4 shows the two representive isotherms: the steep increase of adsorbed volume at low pressures corresponds to the filling micropores and the soft slope for relative pressures between 0.1 and 0.9 is ascribed to the external area of the particles. At P/P₀ > 0.99, the steep volume uptake is attributed to the adsorbate beginning bulk



Fig. 2. IR spectra of iron oxide silica composites prepared from TEOS



Fig. 3. IR spectra of iron oxide silica composites 30/70 prepared from natural silica



Fig. 4. Nitrogen adsorption-desorption isotherm of Fe₂O₃-SiO₂ nanocomposites prepared at 900 °C

condensation to a liquid inside the meso- and macropores formed by the inter particular void.

The isotherm of all samples is open. There are several mechanisms that have been reported as responsible for open isotherm cycles, such activated adsorption arising from a swelling of a silica matrix, restricted access of nitrogen molecules to pores due to blocking at narrow opening, slit-shape pores or a fractal structure expected for silica gels dried under supercritical conditions. The first two cases could be probable for our material: the silica network might have some flexibility because it had narrow opening. Slit-shape pores seem important since the primary particles are spherical and their arrangement determines the pore shape. The adsorbed nitrogen within the microporous particles was in thermodynamic equilibrium during the tested conditions of the isotherm measurement implying that the origin of open cycles may lie on the material itself and not on the measurement conditions [47].

All parameters obtained by means nitrogen adsorption/ desorption method for the all samples are collected in Table-1. The values of surface area of our samples are on the range of $(320-43 \text{ m}^2/\text{g})$. We noticed that the surface area increase with increasing the iron content which is attributed to its heterogeneous composition including pure silica sphere. The mean pore size is higher than 2 nm in all samples. This indicates that type of pore in the supported oxide materials is mesopores [48]. Such pore structure facilitates uniform deposition of iron species within the grains of the support. It is also noticed that pore volume is proportional to the surface area.

TABLE-1 DATA ON POROSITY ANALYSIS BY NITROGEN ADSORPTION/DESORPTION ISOTHERM USING THE BJH

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Samples	Surface area (m ² /g)	Pore volume (cm ³ /g)	Mean pore size (nm)	Open cycle
A2	43.12	0.024	7.123	Yes
B2	97.07	0.045	7.155	Yes
C2	205.7	0.095	7.191	No
N900	6.868	_	_	_

For nanocomposite prepared form natural silica. It is noted that the surface area was decreased compared with the synthetic one. This result can be explained on the basis of particle size effect.

Morphology of iron oxide samples (A2, B2, C2) were studied by scanning electron microscopy. As shown in Fig. 5, the size and homogeneity of particles are independent on the Fe_2O_3 content. The composites obtained exhibits cubic particles, because silica prevent the aggregation of particles. This porosity, which causes increase in surface to volume ratio eventually increase in interaction with heavy metal molecule, is beneficial for surface activity of the film.

Fig. 6 shows the morphology of 30/70 Fe₂O₃/silica. By comparing this sample by the same composition prepared from TEOS, it is found that natural silica led to the aggregation of Fe₂O₃ which result the decrease in surface (this result agree with the measured surface area from BET measurement). So we expect the decrease in interaction between this composite and heavy metals.

Biological study: Natural silica nanoparticles has been found to have several drinking water purification properties.



Fig. 5. SEM image of as prepared Fe₂O₃ annealed at 900 °C



Fig. 6. SEM of Fe₂O₃- SiO₂ nanocomposites(30/70) prepared from natural silica

However, there is no previous study carried out with natural silica nanoparticles and drinking water purification. This mechanism belongs to first line purified natural silica nanoparticles. The demonstrated results might be a base for further studies with natural silica nanoparticles. In addition, the natural silica nanoparticles can be used to decrease the level of heavy metals in drinking water and decrease its effect on the body biomarker analysis.

Data presented in Table-2 represent the levels of serum TC, TG, HDL and LDL concentrations in male rats treated with water purified with natural silica and TEOS at 0.5 and 1.0 g/L.W for 24 h compared to negative control and positive control. There was significant ($p \le 0.05$) alteration in rats exposed to heavy metals (positive control) [49], in comparison to negative control as indicated by significant increases of TC

(+57.44 %), TG (+140.65 %), HDL (-137.3 %) and LDL (+1100.67 %) concentrations. On the other hand, TC, TG, HDL and LDL in groups treated with natural silica and TEOS at 0.5 and 1.0 g/L.W decreased significantly ($p \le 0.05$) compared to positive control. This result may be due to lipid metabolism with the participation of the liver because Majority of fat that builds up in adipose tissue is synthesized in the liver [12].

All the groups administration of natural silica and TEOS at 0.5 and 1.0 g/L.W for 24h were decreased significantly ($p \le$ 0.05) compared to PC in AST, ALT, ALP, y-GT and FBS, respectively (Table-3). Also, AST, ALT, ALP and FBS were increased significantly ($p \le 0.05$) in PC compared to NC [50]. This increase may be due to cellular necrosis of hepatocytes, which causes increase in the permeability of cell resulting release of transaminases and ALP in blood stream [51-53]. Moreover, the increased of serum (ALT and AST) and hyperglycemia indicated metal-induced stressors may be due to influence metabolic pathways in the brain, skeletal muscles and liver, which increased glucose level production and activated gluconeogenesis and glycogenolysis in hepatic cells [54]. Present results agree with several studies who had showed that mercury causes a disturbance in liver function manifested by an increase in serum ALT and AST activity [53], which reflect that the treatment with HgCl₂ caused perturbations in liver function. Cell damage is followed by release of a number of cytoplasmic enzymes to the blood in several organs [55]. Therefore, the increase in ALT and AST activities noted in this study may be explained by the leakage of these enzymes from the liver cytosol into the blood stream. Stacey and Kappaus [56] reported that mercuric chloride intoxication causes significant increase in lipid peroxidation and glucose levels, AST, ALT and ALP activities in liver. The mercury toxic effects involve interaction with a large number of cellular processes, such as the formation of complexes with free thiols and protein thiol groups, which

EFFEC HDI	T OF NATURE AND SYN AND LDL CONCENTRA	TABLE-2 THETIC SILICA GEL NANO TIONS IN MALE RATS TREA	PARTICLES ON SERUM TO ATED WITH HEAVY META	C, TG, LS
Treatment	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
Negative control (NC)	175.3 ± 2.51^{h}	77.0 ± 1.0^{i}	153.7 ± 3.21^{b}	17.3 ± 0.57^{i}
Positive control (PC)	276.0 ± 2.64^{a}	185.3 ± 3.05^{a}	57.33 ± 1.52^{h}	207.6 ± 4.16^{a}
N 900 °C 0.5 g/L.W	$234.6 \pm 4.51^{\circ}$	$136.0 \pm 1.73^{\circ}$	$119.3 \pm 2.51^{\text{f}}$	73.6 ± 1.15^{d}
N 900 °C 1.0 g/L.W	$217.3 \pm 1.52^{\circ}$	$125.3 \pm 3.51^{\circ}$	$123.3 \pm 1.52^{\circ}$	$56.3 \pm 1.15^{\text{f}}$
TEOS 900 °C 0.5 g/L.W	$212.7 \pm 1.52^{\rm f}$	100.6 ± 2.08^{g}	$143.3 \pm 1.52^{\circ}$	46.7 ± 1.53^{g}
TEOS 900 °C 1.0 g/L.W	204.0 ± 3.61^{g}	93.6 ± 1.15^{h}	165.0 ± 3.61^{a}	27.7 ± 0.57^{h}
LSD	4.33113	3.70548	3.57262	3.87138
N = Natural silica gel nanoparticles Statistically significant at (p < 0.05) as compared to NC (One-way ANOVA followed by Fischer's LSD test)				

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EFFECT OF NATURE AND SYNTHETIC SILICA GEL NANOPARTICLES ON SERUM AST, ALT,					
ALP, γ -GT AND FBS CONCENTRATIONS IN MALE RATS TREATED WITH HEAVY METALS					
Treatment	AST (mg/dL)	ALT (mg/dL)	ALP (U/L)	γ-GT (IU/L)	FBS (mg/dL)
Negative control (NC)	25.3 ± 0.57^{d}	42.0 ± 1.73^{a}	110.6 ± 1.15^{i}	28.3 ± 0.57^{d}	$101.0 \pm 1.0^{\rm h}$
Positive control (PC)	54.6 ± 4.9^{a}	43.3 ± 1.52^{a}	184.3 ± 1.15^{a}	44.6 ± 4.9^{a}	144.6 ± 0.5^{a}
N 900 °C 0.5 g/L	32.3 ± 0.1^{b}	43.0 ± 2.0^{a}	$146.6 \pm 1.53^{\circ}$	33.3 ± 0.1^{b}	122.0 ± 1.0^{d}
N 900 °C 1.0 g/L.W	27.3 ± 0.1^{d}	41.6 ± 1.15^{a}	$136.3 \pm 2.88^{\circ}$	28.3 ± 0.1^{d}	121.0 ± 1.0^{d}
TEOS 900 °C 0.5 g/L.W	$38.6 \pm 0.1^{\circ}$	37.0 ± 1.0^{b}	120.6 ± 1.15^{g}	$37.6 \pm 0.1^{\circ}$	$111.3 \pm 0.1^{\text{fg}}$
TEOS 900 °C 1.0 g/L.W	32.3 ± 0.1^{b}	$33.0 \pm 1.73^{\circ}$	113.6 ± 1.53^{h}	30.3 ± 0.1^{d}	109.6 ± 2.1^{g}
LSD	2.91703	2.48765	2.96634	2.61703	1.99109
N = Natural silica nanoparticles Statistically significant at ($p < 0.05$) as compared to negative control (One-way ANOVA followed by Fischer's					

TADLE 2

N = Natural silica nanoparticles Statistically significant at (p < 0.05) as compared to negative control (One-way ANOVA followed by Fischer's LSD test)

may lead to oxidative stress. Due to its sulfhydryl group binding capability, mercuric chloride can also inhibit the activities of many enzymes, especially those involved in the cellular glucose uptake, gluconeogenesis, fatty acid, oxidation and production of glutathione. Further, nickel intoxication caused a significant increase in the activities of GOT, GPT and alkaline phosphatase, probably due to hepatocyte membrane damage resulting in increased release and leakage out of these enzymes from the liver cytosol into the blood stream, which gives an indication on the hepatotoxic effect of this metal. Several studies indicated that an association control exists between nickel toxicity and the increased oxidative stress of rats [57].

Serum CK and LDH were presented in Table-4. CK concentration of blood serum in PC (11.1U/L) decreased significantly ($p \le 0.05$) compared to NC (78.6 U/L). While,

LDH concentration of blood serum in PC increased (1466.6U/ L) significantly ($p \le 0.05$) compared to NC (204.6U/L). Groups treated with natural silica and TEOS (0.05 and 1.0 g/L.W) were increased significantly ($p \le 0.05$) in CK concentration and decreased significantly ($p \le 0.05$) in LDH concentration compared to PC. This results agree with the results indicated by Hardie and Carling [50] they reported that CK concentration of blood serum in PC decreased and LDH concentration increased significantly(p < 0.05) compared to NC. Additionally, LDH indicate increased energy costs associated with raised metabolic activity [54,58,59]. Another study reported that inhibited LDH activities with low and high contaminant exposure is frequently observed in ecotoxicological studies and conforms to the hormetic curve described by Stebbing [54].



Fig. 7. Effects of nature silica and TEOS nanoparticles administration on liver tissue, photomicrographs of sections from liver of various groups of male rats (A-F). (A) Control: rats received distilled water showing normal structure, central vein (V) hepatocytes (H) and sinusoids. (B) Positive control: rats received DWHM showing vacuolation of hepatocytes (V) with congestion of centralvein. (C) nature silica (0.5 g/L.W): rats received water purified by nature silica 0.5 g/L.W showing well developed nuclei (arrow), normal hepatocytes and marked activation of kupffer cells (circle). (D) nature silica (1.0 g/L.W): rats received water purified by nature silica 1.0 g/L.W showing more normal hepatocytes, normal nuclei (arrow) and diffuse kupffer cell proliferation (circle). (E) TEOS (0.5 g/L.W): rats received water purified by TEOS 0.5 g/L.W showing slight coagulative necrosis of the hepatocytes (arrow) and disappearance of the outlines, while the nuclei appeared normal. (F) TEOS (1.0 g/L.W): rats received water purified by TEOS 1.0 g/L.W showing marked activation of kupffer cells (circle) and well developed nuclei (arrow). (x = 40 H & E)

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Treatment	CK (U/L)	LDH (U/L)		
Negative control (NC)	78.6 ± 1.15^{a}	$204.6 \pm 5.6^{\rm f}$		
Positive control (PC)	$11.1 \pm 0.17^{\rm f}$	1466.6 ± 5.8^{a}		
N 900 °C 0.5 g/L	$17.0 \pm 1.0^{\rm e}$	$333.3 \pm 5.7^{\circ}$		
N 900 °C 1.0 g/L.W	19.6 ± 0.58^{cd}	$366.3 \pm 5.5^{\text{b}}$		
TEOS 900 °C 0.5 g/L.W	$20.6 \pm 0.57^{\circ}$	268.3 ± 2.8^{d}		
TEOS 900 °C 1.0 g/L.W	22.6 ± 0.57^{b}	221.0 ± 1.7^{e}		
LSD	1.16723	10.98519		

N = Natural silica nanoparticles Statistically significant at (p < 0.05) as compared to negative control (One-way ANOVA followed by Fischer's LSD test)

Histopathological examination of rat liver: Liver is the target organ of heavy metals toxicity and its cells spell out hepatic enzymes into blood, which are commonly used as biochemical indicator index of hepatocellular damage [57]. The liver samples of DWHM-treated rats showed the focal hepatocytes damage and degeneration (Fig. 7B). It was found that administration of water purified by natural silica and TEOS reversed this liver damage. Water purified by natural silica at a dose of 1.0 g/L.W (Fig. 7D) was more effective when compared with other dose natural silica (0. 05 g/L.W) and TEOS (0.05 and 1.0 g/Lw.) (Fig. 7C,E,F). In present study, the most common observations in liver were vacuolation of hepatocytes with congestion of central vein. These findings are in agree-ment with Durgut et al. [60], these changes may be due to that lead acetate was shown to decrease cytochrome P450 content [61], induces mitogenic response in the rodent liver [62] and glutathione-S-transferase in rat liver [63]. Also, nickel had weak pathological alteration such as the presence of cellular debris within a central vein, cytological vacuolization, dilated sinusoids and the appearance of hepatic cells with distorted nuclei in liver. Accordingly, biochemical perturbations (ALT, AST and ALP) seem to be correlated with the liver histological alteration and a cytoplasmic vacuolization [64].

ACKNOWLEDGEMENTS

This research project is funded by University of Dammam, Damma, Saudi Arabia Grant No. 2012021. The authors are grateful for the assistance of Field Crop Technology Research Department, Food Technology Research Institute, Agricultural Research Center, Giza, Egypt.

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