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1.1. Iron intake increases infarct volume alter permanent middle cerebral artery occlusion in rats

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Research report

Iron intake increases infarct volume after permanent middle cerebral artery occlusion in rats☆

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Abstract

Experimental and clinical data suggest an important role of iron in cerebral ischaemia. We measured infarct volume and analysed the oxidative stress, and also the excitatory and inflammatory responses to brain injury in a rat stroke model after an increased oral iron intake. Permanent middle cerebral artery occlusion (MCAO) was performed in ten male Wistar rats fed with a diet containing 2.5% carbonyl iron for 9 weeks, and in ten control animals. Glutamate, interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α) were determined in blood samples before and at 2, 4, 6, 8, 24 and 48 h after MCAO, and thiobarbituric acid reaction substances (TBARS) were analysed at 48 h. Infarct volume was measured at 48 h by image analysis on brain slices stained with 1% TTC. Tissue iron was measured by atomic absorption spectrophotometry. Infarct volume was 66% greater in the iron fed rats than in the control group (178±49 mm^3 versus 107±53 mm^3, $P<0.01$). Significant higher levels of glutamate, IL-6 and TNF-α were observed in the group with iron intake (peak values were obtained at 6, 8 and 4 h, respectively). Iron-fed animals also showed significantly higher levels of TBARS than those receiving a normal diet (6.52±0.59 vs. 5.62±0.86 μmol/l, $P=0.033$) Liver iron stores (3500±199 vs. 352±28 μg Fe/g, $P<0.0001$), but not brain iron stores (131 vs. 139 μg Fe/g, $P=0.617$), were significantly higher in the iron fed rats group. These results suggest that iron intake is associated with larger infarct volumes after MCAO in the rat. This effect seems to be associated with higher oxidative stress, excitotoxicity and inflammatory responses.

Theme: Development and regeneration

Topic: Nutritional and prenatal factors

Keywords: Iron; Infarct volume; Glutamate; Cytokine; Stroke model; Rat

1. Introduction

In the last few years, research into the pathogenic factors associated with cerebral ischaemia has established that excitotoxicity, free radicals, and inflammation participate in brain injury secondary to hypoxia [11,16,37,40]. These mechanisms both interact and act sequentially to provide a common pathway for cell vulnerability in the ischaemic brain [41].

Iron-mediated free radical generation plays a key role in ischaemic brain injury. Free iron catalyses the Haber–Weiss reaction, resulting in the formation of the hydroxyl free radical, one of the most important mediators of tissue injury in ischaemia–reperfusion [38]. Experimental studies in gerbils have found that, shortly after stroke onset, changes in iron metabolism related proteins take place, promoting the release of free iron in the ischaemic tissue [18]. Feeding gerbils with an iron-deficient diet until iron tissue stores were depleted, had the effect of attenuating brain oedema following focal cerebral ischaemia and

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reperfusion, and this same effect was observed after giving gerbils fed with a normal diet a dose of deferoxamine before reperfusion [31].

The role of tissue iron stores seems crucial since clinical studies have found evidence of iron-related brain damage in patients with acute ischaemic stroke. Plasma and CSF ferritin concentrations were significantly higher within the first 24 h after stroke onset in patients with subsequent early neurological deterioration, larger infarct volumes, and poor outcome at 1 month [8,9]. Heterozygous haemochromatosis could be a common cause of iron overload in humans [28,42] although, with the exception of those areas in which the blood–brain barrier (BBB) is lacking, high amounts of iron are not found in the brain [19]. It is therefore unclear whether increased iron stores in brain tissue contribute to poor prognosis in acute stroke.

The mechanisms involved in ischaemic brain injury related to iron overload are unknown, and the effect of increased iron intake on infarct size has not been established. The aim of this study was to measure infarct volume and to evaluate the oxidative stress and the excitatory and inflammatory responses in blood to cerebral ischaemia in a permanent middle cerebral artery occlusion (MCAO) model in rats after increased oral iron intake.

2. Materials and methods

2.1. Animals

Ten male Wistar rats, after a 4-week weaning period, were fed with a standard diet containing 0.012% of ferric citrate (AIN-93G Diet of the American Institute of Nutrition; ICN) supplemented with 2.5% w/w carbonyl iron (Sigma) for 9 weeks (each gram of diet contained approximately 25 mg of iron), and ten control animals received the standard diet without iron supplementation during the same period. Diet and tap water was given ad libitum up to 24 h before MCAO rats were operated on. Adequate measures were taken to minimise pain or discomfort of the animals.

2.2. Model of ischaemia

Male Wistar rats weighing 372±43.5 g (control group) and 329±24.2 g (iron-fed rat group) were anaesthetised with an intraperitoneal injection of pentobarbital (60 mg/kg). Ipsilateral common carotid artery ligation was carried out in order to improve the reproducibility of infarction. The skin and temporal muscle were cut and craniotomy was performed exposing the left MCA transcranially. After making a cut in the dura mater, the MCA was lifted off distally and occluded by electrocoagulation using fine bipolar forceps (Erbe, ICC50, Germany). The artery was then transected to avoid recanalisation. Body temperature was kept at around 37 °C during the entire surgical process.

Two rats fed with the standard diet died 1 h and between 24 and 48 h after the operation, but none of the rats fed with iron supplements.

2.3. Blood sample collection

Blood tail samples (0.4 ml) were taken before and at 2, 4, 6, 8, 24, and 48 h after MCAO. The corresponding plasma or serum was obtained by centrifugation at 3000×*g* for 5 min, and stored at −80 °C until the biochemical determinations were made. Plasma glucose, haematocrit, haemoglobin, and total serum proteins were measured in the baseline samples, and glucose determinations were repeated at 4, 24 and 48 h after MCAO. Plasma total iron, total iron binding capacity (TIBC), and ferritin were measured at 48 h.

2.4. Measurement of infarct volume

After the final blood sample was taken, the anaesthetised animals were perfused through the heart with a phosphate buffer (pH 7.4) with 0.01% heparin to remove all the blood. Immediately afterwards, the livers were removed and stored at −80 °C until analysis. Brains were also removed from the skulls and series of 2 mm coronal brain slices were obtained and stained with 1% TTC (2,3,5-triphenyl-tetrazolium chloride, Merck) in order to obtain images of the brain infarction. The brain slices were then immersed in 4% paraformaldehyde in phosphate buffer for 48 h to perform histological iron staining.

Infarct volume was quantified by image analysis (Visilog 5.0 Noesis 1996, Spain).

2.5. Measurement of tissue iron levels in brain and liver

The total iron in liver and brain was measured by atomic absorption spectrometry (AAS), after acid digestion of organic samples, as described by Verlinden [45]. Briefly, tissue samples were dried at 110 °C. Accurately weighed 0.5 g samples of dry material were placed into 250 ml Pyrex digestion tubes (diameter 42 mm, height 30 cm) and 25 ml of concentrated nitric acid was added. Air-condensers were fitted to the tubes and the mixture was left to stand overnight at 60 °C in a temperature-controlled heated aluminium block. Then, the mixture was heated at 120 °C for 1 h. The condensers were then removed and the volume was reduced to 5 ml by heating at 140 °C (the tubes were surrounded by an aluminium shield to protect them against air cooling) and then allowed to cool. Five millilitres of perchloride acid concentrate was added and the condensers were fitted before heating at 220 °C for 30 min. After the removal of the condensers and evaporation to 2 ml, the solutions were completely clear. The solution was then transferred to 20-ml volumetric flasks and diluted with deionised water to the required volume. The iron content of the digested acid was measured at 248 nm using a

Unicam PU-9200X flame atomic absorption spectrometer with deuterium lamp correction against ferric chloride standards diluted in 0.5% hydrochloric acid. The method, which meets international standards, has been used in our laboratory for 10 years.

2.6. Histological staining for iron

Coronal slabs of the cerebrum, cerebellum and brain stem were embedded in paraffin and cut with a sliding microtome. Sections, 5 μm thick, were stained following the Perls' method (potassium ferricyanide and 5% HCl) intensified with diaminobenzidine (DAB) and nickel by which iron deposition is recognised as a blue-green precipitate. Human dentate nucleus with pigment and iron deposition was used as a control and was also processed.

2.7. Iron and related proteins in blood

Plasma iron and TIBC were determined following the method of Fielding [14] which was modified to use 100 μl of sample. Plasma iron and supernatant iron content were measured by graphite furnace atomic absorption at 372.0 nm with a Varian spectra A30 Zeeman spectrometer (Victoria, Australia). Calibration was made by standard additions of a concentrate of 100 ng Fe/ml in 1% nitric acid. The glassware used for the preparation of standard solutions and for the testing of iron was soaked in 0.75 mol/l nitric acid and rinsed with deionised purified water.

Plasma ferritin concentration was determined by using enzyme-linked immunosorbent assay (ELISA) with coated tubes as the solid phase. Rabbit anti-rat liver antibody and streptavidin technology were used. Rat liver ferritin antibodies were obtained from New Zealand rabbits and purified from the antisera by affinity chromatography as previously described [35]. Purified antibodies were then biotinylated [4] and coupling of horseradish peroxidase to the antibodies was performed essentially using the procedure of Ghielmi et al. [15]. Rat liver ferritin (Sigma) was used as standard. Enzymatic activity was determined with a microplate reader (Labsystems) using ABTS as substrate. Absorbance was measured at 405 nm.

2.8. Measurement of lipid peroxidation

At 48 h, lipid peroxidation was determined by measuring the levels of thiobarbituric acid reaction substances (TBARS) in serum following the method of Yagi et al. [48]. In order to isolate lipids, 50 μl of serum was precipitated using sulphuric/phosphotungstic acid. After centrifuging, the supernatant was discarded and the sediment resuspended in 0.4 ml of distilled water. To avoid artefact oxidation, EDTA and BHT were added. 0.1 ml of TBA reagent (1% of TBA in equal volumes of aqueous solution and glacial acetic acid) was also added and mixed. The resulting mixture was heated at 95 °C for 60 min. After cooling, *n*-butanol was added, shaken and the butanol layer separated by centrifugation. The optical density of the butanol layer was read at 540–620 nm. A standard MDA curve was obtained by acid hydrolysis of tetraethoxypropane.

2.9. Testing for amino acids and pro-inflammatory molecules

Glutamate and glycine were quantified by the cation exchange chromatography method using a LKB/4151 Alpha Plus autoanalyser (Bromma, Uppsala, Sweden), as previously described [24]. Interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α) concentrations in serum were measured with commercially available quantitative sandwich enzyme-linked immunosorbent assay (Quantikine) kits, from R&D Systems (Minneapolis, MN, USA). Amino acid and cytokine determinations were performed with blinding to diet type and the other experimental results.

2.10. Statistical analysis

The analytic values and the infarct volumes are presented as mean±S.D. The significance was calculated by the Student *t*-test. Differences were considered statistically significant at $P<0.05$.

3. Results

Prior to the MCAO, and during the procedure, both groups of animals showed similar body weight, haematocrit, serum glucose, and total proteins (Table 1). Infarct volume was 66% greater in iron fed rats than in control animals (178 ± 49 mm^3 vs. 107 ± 53 mm^3, $P<0.01$). The infarcted area was located in the ipsilateral cerebral cortex, but a slight extension to the striatum (0.5% to 1%) was observed in both groups.

3.1. Biochemical studies

Plasma iron levels and TIBC values were not sig-

Table 1
Physiological parameters by groups of animals

	Iron diet supplementation (*n*=10)	Normal diet (*n*=10)
Body weight, g	329±24.2	372±43.5
Serum glucose, g/dl	82.2±24.4	99.9±17.8
Serum total proteins, g/dl	5.9±0.4	5.6±0.5
Haematocrit, %	41.6±2.5	44.7±3.4
Haemoglobin, g/dl	15.6±1.6	16.2±2.3
Plasma iron, μg/dl	274±48	310±36
TIBC, μg/dl	436±17	523±22
Plasma ferritin, ng/ml	3130±547	626±107**
TBARS, μmol/l	6.5±0.6	5.6±0.8*

Values are expressed as mean±S.D. *$P<0.05$; **$P=0.001$.

nificantly different between the control group and the group of rats fed with iron, but plasma ferritin concentration was higher in the iron fed animals ($P=0.001$). This group also showed significantly higher levels of TBARS than the group receiving a normal diet ($P=0.033$) (Table 1).

Fig. 1 shows the serum concentrations of amino acid and cytokines at baseline and at different times after MCAO in iron fed rats and the control group. Baseline levels of glutamate, IL-6 and TNF-α showed a sharp increase at 6, 8, and 4 h after MCAO, respectively. Peak values were found at 8 h in the case of glutamate and IL-6, and at 6 h for TNF-α. The concentrations of glutamate and cytokines in the group of rats fed with iron were significantly higher than in the control group from 4 h after the onset of ischaemia in the case of glutamate and TNF-α, and from 2 h in the case of IL-6. These differences were maintained throughout all the determinations.

Atomic absorption spectrophotometric analysis showed that liver non-haem iron stores (3501 ± 199 vs. 352 ± 28 μg Fe/g of tissue, $P<0.0001$), but not brain non-haem iron stores (131 ± 11 vs. 139 ± 8 μg Fe/g of tissue, $P=0.617$), were significantly higher in rats fed with iron than in the control group.

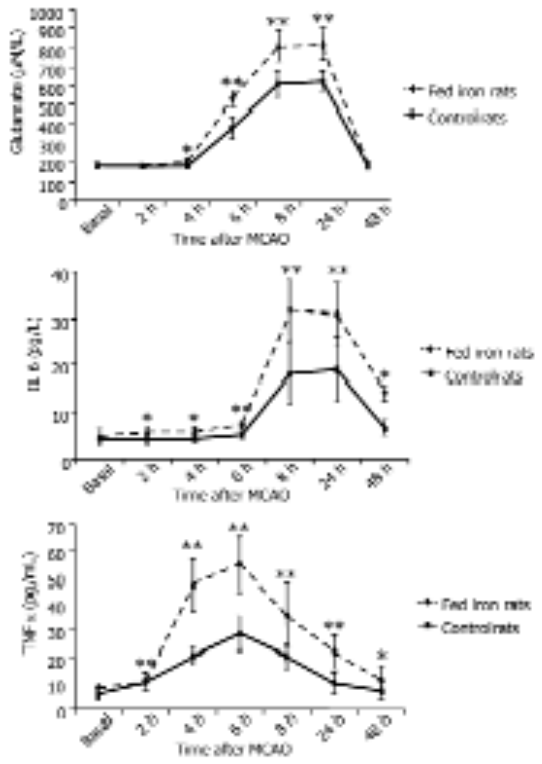

Fig. 1. Serum levels of glutamate, interleukin-6, and tumour necrosis factor-α at different time intervals after permanent middle cerebral artery occlusion in rats fed with iron (solid line) and with a standard diet (dotted line). Symbols and vertical lines represent the mean and S.D. values of biochemical concentrations (Student's *t*-test, *$P<0.01$; **$P<0.001$).

3.2. Histological analyses

No iron deposits were found in the brains of animals after MCAO. Particular attention was paid to the possible differences between ischaemic and non-ischaemic areas, as well as among different brain regions covering the striatum, pallidus, cerebral cortex and cerebellum and deep cerebellar nuclei.

4. Discussion

This study demonstrates that brain infarctions after permanent MCAO are 66% greater in rats fed with iron than in control animals, and hence supports the hypothesis that iron plays an important role in ischaemic brain injury. To the best of our knowledge, only one previous study has assessed the role of dietary iron content in cerebral ischaemia. In this study, gerbils fed with a low-iron diet for 8 weeks had decreased brain and serum iron levels, less neurological deficits and attenuated brain oedema after temporary unilateral carotid ligation and reperfusion than gerbils fed with a control standard diet [31]. However, the effect of an increase in iron intake on the ischaemic brain has not been examined in experimental studies.

The mechanisms by which iron contributes to ischaemic brain injury seem to be primarily related to its participation as a mediator in oxidative stress reactions [20,39]. Free iron catalyses the generation of free radicals, leading to cellular membrane disruption and cerebral oedema by lipid peroxidation of polyunsaturated fatty acids [40]. In fact, our animals fed with an iron supplemented diet showed significantly higher levels of TBARS, which suggests that iron plays a role in the process of lipid peroxidation. Levels of glutamate and pro-inflammatory molecules in blood, which were similar in both groups of animals at baseline, turn out to be significantly higher in the iron fed rats after MCAO. Although the relationship between the changes in blood and brain of these molecules has not been established, plasma glutamate increase occurs as a result of the ischaemic brain injury, since plasma glutamate levels are not modified in sham operated animals [34]. These findings suggest that the greater infarct volume after iron intake may be related to an enhanced iron-mediated excitotoxic and inflammatory response.

The blood chemical changes observed in this study agree with the metabolic events found in cerebral ischaemia. Recent studies have suggested an important interrelation between iron-catalysed free radical generation and excitatory amino acid (EAA) release in ischaemic brain injury [22,23,27]. Some authors have hypothesised that free radicals and EAAs may be involved in a vicious

circle in which each helps the other to generate and propagate ischaemic neuronal death [32]. In this respect, parallel iron chelation and anti-excitotoxic therapy improves outcome after incomplete cerebral ischaemia [10]. A potential interaction between body iron stores and excitotoxicity has also been suggested as a mechanism of early neurological worsening in humans with acute ischaemic stroke [8]. On the other hand, free radicals generated on the endothelial cell surface by ischaemia/reperfusion activate the inflammatory response [36]. The local expression of inflammatory cytokines results in chemotactic cytokine release, leukocyte adhesion molecules up-regulation, and conversion of the local endothelium to a prothrombotic state [21,24,25]. Increases in pro-inflammatory cytokines (IL-1, TNF-α and IL-6) have been detected in the ischaemic cortex 1 h after MCAO in experimental models [49], while an increase in infarct volume and brain oedema have been demonstrated experimentally after intraventricular injection of IL-1 and TNF-α [2,49]. Many clinical studies have reported increases in the levels of pro-inflammatory cytokines in peripheral blood and CSF in patients with acute ischaemic stroke [3,12,13,43,46].

An intriguing feature of this study is that the effect of iron on infarct volume was not associated with greater iron stores in the normal brain. Neither spectrophotometric assays nor histological analyses showed differences between iron fed animals and controls. This fact was not the consequence of a limited absorption of iron since plasma ferritin levels and liver iron concentrations were 5 to 10 times higher in iron fed animals. Similarly, other authors have found that dietary iron overload in rats produces a significant dose-related increase of non-haem iron in liver, but no significant accumulation of iron is found in the brain [7,30,45,47]. This result is likely due to the constitution of the BBB and blood–CSF barrier around the 21st day of life, which protect the brain against the influx of iron from the systemic circulation. Our data are consistent with these findings since we fed rats with iron after a weaning period of 4 weeks. After this age, the influx of iron is regulated by a transferrin receptor-mediated transport, and such receptors, which are located in the capillary endothelium, are down-regulated by the iron excess in diet [33,44]. In the present study, we paid special attention to the histological analysis of brain areas in which rats show the highest concentrations of iron, i.e. globus pallidus, substantia nigra, interpeduncular nuclei and dentate gyrus [17], but no differences were found between the two groups of animals. Therefore, the effect of iron overload in infarct volume would not seem to be explained by a direct toxic action resulting from iron accumulation in the brain parenchyma.

An alternative hypothesis to explain the iron effect in this model may be related to the disruption of the permeability of brain barriers by the ischaemic process [2,29], which results in the loss of the protecting effect that these barriers exert on brain tissues [1]. Once the cerebral endothelium has been damaged by ischaemia, high ferritin iron plasma concentrations, or of other forms of non-transferrin iron [5] might have access to the lipid-rich neuronal environment enhancing the inflammatory and oxidative stress responses in brain tissue [6]. Furthermore, the hydroxyl radical generated in endothelial and smooth muscle cells through the iron-catalysed Haber–Weiss reaction may have an additional role in disrupting the BBB and promoting brain oedema [26]. Overall, these effects could be responsible for the greater infarct volume found in this study in rats with increased iron intake. We can thoughtfully rule out that larger infarct volumes in iron fed animals were due to distinct metabolic or hemodynamic systemic disturbances. There were no differences in body temperature and serum glucose between the two groups during the experiment, and haematocrit values and total protein levels were found to be similar. Although myocardial function may be altered as a result of iron overload [12], no data suggested heart damage in this study.

In conclusion, we have demonstrated that increased oral iron intake causes larger infarct volumes after permanent MCAO in rats, and that this effect is associated with higher oxidative stress, excitotoxicity and inflammatory responses. The underlying mechanisms of iron-related brain injury do not seem linked to increased iron stores in the normal brain.

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CAPÍTULO 2:
FICHAS TÉCNICAS

2.1. Ácido Clorhídrico

Fichas Internacionales de Seguridad Química

CLORURO DE HIDROGENO ICSC: 0163

MINISTERIO DE TRABAJO Y ASUNTOS SOCIALES ESPAÑA

INSTITUTO NACIONAL DE SEGURIDAD E HIGIENE EN EL TRABAJO

CLORURO DE HIDROGENO
Acido clorhídrico, anhidro
Cloruro de hidrógeno, anhidro
HCl
Masa molecular: 36.5

Nº CAS 7647-01-0
Nº RTECS MW4025000
Nº ICSC 0163
Nº NU 1050
Nº CE 017-002-00-2

TIPOS DE PELIGRO/ EXPOSICION	PELIGROS/ SINTOMAS AGUDOS	PREVENCION	PRIMEROS AUXILIOS/ LUCHA CONTRA INCENDIOS
INCENDIO	No combustible.		En caso de incendio en el entorno: están permitidos todos los agentes extintores.
EXPLOSION			En caso de incendio: mantener fría la botella rociando con agua pero NO en contacto directo con agua.
EXPOSICION		¡EVITAR TODO CONTACTO!	¡CONSULTAR AL MEDICO EN TODOS LOS CASOS!
• INHALACION	Corrosivo. Sensación de quemazón, tos, dificultad respiratoria, jadeo, dolor de garganta. (Síntomas no inmediatos: véanse Notas).	Ventilación, extracción localizada o protección respiratoria.	Aire limpio, reposo, posición de semiincorporado, respiración artificial si estuviera indicada y proporcionar asistencia médica.
• PIEL	Corrosivo. Quemaduras cutáneas graves, dolor.	Guantes protectores y traje de protección.	Quitar las ropas contaminadas, aclarar la piel con agua abundante o ducharse y proporcionar asistencia médica.
• OJOS	Corrosivo. Dolor, visión borrosa, quemaduras profundas graves.	Gafas ajustadas de seguridad, pantalla facial o protección ocular combinada con la protección respiratoria.	Enjuagar con agua abundante durante varios minutos (quitar las lentes de contacto si puede hacerse con facilidad) y proporcionar asistencia médica.
• INGESTION			

DERRAMAS Y FUGAS	ALMACENAMIENTO	ENVASADO Y ETIQUETADO
Evacuar la zona de peligro. Consultar a un experto. Ventilar. Eliminar gas con agua pulverizada. (Protección personal adicional: traje de protección completa incluyendo equipo autónomo de repiración).	Separado de sustancias combustibles y reductoras, oxidantes fuertes, bases fuertes, metales. Mantener en lugar bien ventilado.	CE: símbolo C símbolo T R: 23-35 S: (1/2-)9-26-36/37/39-45 Clasificación de Peligros NU: 2.3 Riesgos Subsidiarios NU: 8

VEASE AL DORSO INFORMACION IMPORTANTE

ICSC: 0163

Fichas Internacionales de Seguridad Química

CLORURO DE HIDROGENO

ICSC: 0163

DATOS IMPORTANTES

ESTADO FISICO; ASPECTO
Gas licuado comprimido incoloro, de olor acre.

PELIGROS FISICOS
El gas es más denso que el aire.

PELIGROS QUIMICOS
La disolución en agua es un ácido fuerte, reacciona violentamente con bases y es corrosiva. Reacciona violentamente con oxidantes formado gas tóxico de cloro. En contacto con el aire desprende humos corrosivos de cloruro de hidrógeno. Ataca a muchos metales formando hidrógeno.

LIMITES DE EXPOSICION
TLV: 5 ppm; 7.5 mg/m^3 (valor techo) (ACGIH 1993-1994).

VIAS DE EXPOSICION
La sustancia se puede absorber por inhalación.

RIESGO DE INHALACION
Al producirse una pérdida de gas se alcanza muy rápidamente una concentración nociva de éste en el aire.

EFECTOS DE EXPOSICION DE CORTA DURACION
Corrosivo. La sustancia es corrosiva de los ojos, la piel y el tracto respiratorio. La inhalación de altas concentraciones del gas puede originar edema pulmonar (véanse Notas). Los efectos pueden aparecer de forma no inmediata.

EFECTOS DE EXPOSICION PROLONGADA O REPETIDA
La sustancia puede afectar el pulmón, dando lugar a bronquitis crónica. La sustancia puede causar erosiones dentales.

PROPIEDADES FISICAS

Punto de ebullición a 101.3 kPa: -85°C
Punto de fusión: -114°C
Solubilidad en agua, g/100 ml a 20°C: 72

Solubilidad en agua: Elevada
Densidad relativa de vapor (aire = 1): 1.3
Coeficiente de reparto octanol/agua como log Pow: 0.25

DATOS AMBIENTALES

NOTAS

El valor límite de exposición laboral aplicable no debe superarse en ningún momento de la exposición en el trabajo. Los síntomas del edema pulmonar no se ponen de manifiesto, a menudo, hasta pasadas algunas horas y se agravan por el esfuerzo físico. Reposo y vigilancia médica son por ello, imprescindibles. Debe considerarse la inmediata administración de un aerosol adecuado por un médico o persona por él autorizada. NO pulverizar con agua sobre la botella que tenga un escape (para evitar la corrosión de la misma). Con el fin de evitar la fuga de gas en estado líquido, girar la botella que tenga un escape manteniendo arriba el punto de escape.

Ficha de emergencia de transporte (Transport Emergency Card): TEC (R)-135
Código NFPA: H 3; F 0; R 0;

INFORMACION ADICIONAL

FISQ: 3-072 CLORURO DE HIDROGENO

ICSC: 0163 **CLORURO DE HIDROGENO**

2.2. Hidróxido de sodio

Fichas Internacionales de Seguridad Química

HIDROXIDO DE SODIO **ICSC: 0360**

MINISTERIO DE TRABAJO Y ASUNTOS SOCIALES ESPAÑA

INSTITUTO NACIONAL DE SEGURIDAD E HIGIENE EN EL TRABAJO

HIDROXIDO DE SODIO
Hidróxido sódico
Sosa cáustica
Sosa
NaOH
Masa molecular: 40.0

Nº CAS 1310-73-2
Nº RTECS WB4900000
Nº ICSC 0360
Nº NU 1823
Nº CE 011-002-00-6

TIPOS DE PELIGRO/ EXPOSICION	PELIGROS/ SINTOMAS AGUDOS	PREVENCION	PRIMEROS AUXILIOS/ LUCHA CONTRA INCENDIOS
INCENDIO	No combustible. El contacto con la humedad o con el agua, puede generar el suficiente calor para producir la ignicion de sustancias combustibles.		En caso de incendio en el entorno: están permitidos todos los agentes extintores.
EXPLOSION			
EXPOSICION		¡EVITAR LA DISPERSION DEL POLVO! ¡EVITAR TODO CONTACTO!	¡CONSULTAR AL MEDICO EN TODOS LOS CASOS!
• INHALACION	Corrosivo. Sensación de quemazón, tos, dificultad respiratoria.	Extracción localizada o protección respiratoria.	Aire limpio, reposo, posición de semiincorporado, respiración artificial si estuviera indicada y proporcionar asistencia médica.
• PIEL	Corrosivo. Enrojecimiento, graves quemaduras cutáneas, dolor.	Guantes protectores y traje de protección.	Quitar las ropas contaminadas, aclarar la piel con agua abundante o ducharse y proporcionar asistencia médica.
• OJOS	Corrosivo. Enrojecimiento, dolor, visión borrosa, quemaduras profundas graves.	Pantalla facial o protección ocular combinada con la protección respiratoria si se trata de polvo.	Enjuagar con agua abundante durante varios minutos (quitar las lentes de contacto si puede hacerse con facilidad) y proporcionar asistencia médica.
• INGESTION	Corrosivo. Dolor abdominal, sensación de quemazón, diarrea, vómitos, colapso.	No comer, ni beber ni fumar durante el trabajo.	Enjuagar la boca, NO provocar el vómito, dar a beber agua abundante y proporcionar asistencia médica.

DERRAMAS Y FUGAS	ALMACENAMIENTO	ENVASADO Y ETIQUETADO
Barrer la sustancia derramada e introducirla en un recipiente adecuado, eliminar el residuo con agua abundante. (Protección personal adicional: traje de protección completa incluyendo equipo autónomo de respiración).	Separado de ácidos fuertes, metales, alimentos y piensos, materiales combustibles. Mantener en lugar seco y bien cerrado (véanse Notas).	No transportar con alimentos y piensos. símbolo C R: 35 S: (1/2-)26-37/39-45 Clasificación de Peligros NU: 8 Grupo de Envasado NU: II

VEASE AL DORSO INFORMACION IMPORTANTE

ICSC: 0360	Preparada en el Contexto de Cooperación entre el IPCS y la Comisión de las Comunidades Europeas © CCE, IPCS, 1994

Fichas Internacionales de Seguridad Química

HIDROXIDO DE SODIO

ICSC: 0360

DATOS IMPORTANTES	**ESTADO FISICO; ASPECTO** Sólido blanco, delicuescente en diversas formas e inodoro. **PELIGROS FISICOS** **PELIGROS QUIMICOS** La sustancia es una base fuerte, reacciona violentamente con ácidos y es corrosiva en ambientes húmedos para metales tales como cinc, aluminio, estaño y plomo originando hidrógeno (combustible y explosivo). Ataca a algunas formas de plástico, de caucho y de recubrimientos. Absorbe rápidamente dióxido de carbono y agua del aire. Puede generar calor en contacto con la humedad o el agua. **LIMITES DE EXPOSICION** TLV: 2 mg/m^3 (valor techo) (ACGIH 1992-1993). PDK no establecido. MAK: clase G	**VIAS DE EXPOSICION** La sustancia se puede absorber por inhalación del aerosol y por ingestión. **RIESGO DE INHALACION** La evaporación a 20°C es despreciable; sin embargo, se puede alcanzar rápidamente una concentración nociva de partículas en el aire. **EFECTOS DE EXPOSICION DE CORTA DURACION** Corrosivo. La sustancia es muy corrosiva de los ojos, la piel y el tracto respiratorio. Corrosivo por ingestión. La inhalación del aerosol de la sustancia puede originar edema pulmonar (véanse Notas). **EFECTOS DE EXPOSICION PROLONGADA O REPETIDA** El contacto prolongado o repetido con la piel puede producir dermatitis.
PROPIEDADES FISICAS	Punto de ebullición: 1390°C Punto de fusión: 318°C Densidad relativa (agua = 1): 2.1	Solubilidad en agua, g/100 ml a 20°C: 109 Presión de vapor, kPa a 739°C: 0.13
DATOS AMBIENTALES	Esta sustancia puede ser peligrosa para el ambiente; debería prestarse atención especial a los organismos acuáticos.	

NOTAS

El valor límite de exposición laboral aplicable no debe superarse en ningún momento de la exposición en el trabajo. Los síntomas del edema pulmonar no se ponen de manifiesto, a menudo, hasta pasadas algunas horas y se agravan por el esfuerzo físico. Reposo y vigilancia médica son por ello, imprescindibles. NO verter NUNCA agua sobre esta sustancia; cuando se deba disolver o diluir, añadirla al agua siempre lentamente. Almacenar en una área que disponga de un suelo de hormigón, resistente a la corrosión.

Ficha de emergencia de transporte (Transport Emergency Card): TEC (R)-121
Código NFPA: H 3; F 0; R 1;

INFORMACION ADICIONAL

FISQ: 3-134 HIDROXIDO DE SODIO

2.3. Glucosa

Fichas Internacionales de Seguridad Química

GLUCOSA ICSC: 0865

MINISTERIO DE TRABAJO Y ASUNTOS SOCIALES ESPAÑA

INSTITUTO NACIONAL DE SEGURIDAD E HIGIENE EN EL TRABAJO

GLUCOSA
Dextrosa
Azúcar de uva
$C_6H_{12}O_6$
Masa molecular: 180.16

N° CAS 50-99-7
N° RTECS LZ6600000
N° ICSC 0865

TIPOS DE PELIGRO/ EXPOSICION	PELIGROS/ SINTOMAS AGUDOS	PREVENCION	PRIMEROS AUXILIOS/ LUCHA CONTRA INCENDIOS
INCENDIO	Combustible.		Polvos, pulverización con agua, espuma, dióxido de carbono.
EXPLOSION			
EXPOSICION			
• INHALACION	Tos.	Ventilación.	Aire limpio, reposo.
• PIEL			
• OJOS	Enrojecimiento.	Gafas ajustadas de seguridad.	Enjuagar con agua abundante durante varios minutos (quitar las lentes de contacto si puede hacerse con facilidad), después consultar a un médico.
• INGESTION			Enjuagar la boca.

DERRAMAS Y FUGAS	ALMACENAMIENTO	ENVASADO Y ETIQUETADO
Barrer la sustancia derramada e introducirla en un recipiente, eliminar el residuo con agua abundante.	Mantener en lugar seco.	

VEASE AL DORSO INFORMACION IMPORTANTE

ICSC: 0865 Preparada en el Contexto de Cooperación entre el IPCS y la Comisión de las Comunidades Europeas © CCE, IPCS, 1994

Fichas Internacionales de Seguridad Química

GLUCOSA ICSC: 0865

Fichas Internacionales de Seguridad Química

GLUCOSA ICSC: 0865

MINISTERIO DE TRABAJO Y ASUNTOS SOCIALES ESPAÑA

INSTITUTO NACIONAL DE SEGURIDAD E HIGIENE EN EL TRABAJO

GLUCOSA
Dextrosa
Azúcar de uva
$C_6H_{12}O_6$
Masa molecular: 180.16

N° CAS 50-99-7
N° RTECS LZ6600000
N° ICSC 0865

TIPOS DE PELIGRO/ EXPOSICION	PELIGROS/ SINTOMAS AGUDOS	PREVENCION	PRIMEROS AUXILIOS/ LUCHA CONTRA INCENDIOS
INCENDIO	Combustible.		Polvos, pulverización con agua, espuma, dióxido de carbono.
EXPLOSION			
EXPOSICION			
• INHALACION	Tos.	Ventilación.	Aire limpio, reposo.
• PIEL			
• OJOS	Enrojecimiento.	Gafas ajustadas de seguridad.	Enjuagar con agua abundante durante varios minutos (quitar las lentes de contacto si puede hacerse con facilidad), después consultar a un médico.
• INGESTION			Enjuagar la boca.

DERRAMAS Y FUGAS	ALMACENAMIENTO	ENVASADO Y ETIQUETADO
Barrer la sustancia derramada e introducirla en un recipiente, eliminar el residuo con agua abundante.	Mantener en lugar seco.	

VEASE AL DORSO INFORMACION IMPORTANTE

ICSC: 0865 Preparada en el Contexto de Cooperación entre el IPCS y la Comisión de las Comunidades Europeas © CCE, IPCS, 1994

Fichas Internacionales de Seguridad Química

GLUCOSA ICSC: 0865

2.4. Permanganato de potasio

Fichas Internacionales de Seguridad Química

PERMANGANATO DE POTASIO **ICSC: 0672**

MINISTERIO DE TRABAJO Y ASUNTOS SOCIALES ESPAÑA

INSTITUTO NACIONAL DE SEGURIDAD E HIGIENE EN EL TRABAJO

$KMnO_4$

Masa molecular: 158

Nº ICSC 0672
Nº CAS 7722-64-7
Nº RTECS SD6475000
Nº NU 1490
Nº CE 025-002-00-9

TIPOS DE PELIGRO/ EXPOSICION	PELIGROS/ SINTOMAS AGUDOS	PREVENCION	PRIMEROS AUXILIOS/ LUCHA CONTRA INCENDIOS
INCENDIO	No combustible pero facilita la combustión de otras sustancias. En caso de incendio se desprenden humos (o gases) tóxicos e irritantes.	NO poner en contacto con sustancias inflamables.	En caso de incendio en el entorno: están permitidos todos los agentes extintores.
EXPLOSION	Riesgo de incendio y explosión en contacto con sustancias combustibles yagentes reductores.		
EXPOSICION		¡EVITAR LA DISPERSION DEL POLVO! ¡HIGIENE ESTRICTA!	
• INHALACION	Sensación de quemazón. Tos. Dolor de garganta. Jadeo. Dificultad respiratoria. Síntomas no inmediatos (véanse Notas).	Evitar la inhalación del polvo . Extracción localizada o protección respiratoria.	Aire limpio, reposo. Posición de semiincorporado. Respiración artificial si estuviera indicada. Proporcionar asistencia médica.
• PIEL	Enrojecimiento. Quemaduras cutáneas. Dolor.	Guantes protectores. Traje de protección.	Aclarar con agua abundante, después quitar la ropa contaminada y aclarar de nuevo. Proporcionar asistencia médica.
• OJOS	Enrojecimiento. Dolor. Quemaduras profundas graves.	Pantalla facial, o protección ocular combinada con la protección respiratoria.	Enjuagar con agua abundante durante varios minutos (quitar las lentes de contacto si puede hacerse con facilidad), después proporcionar asistencia médica.
• INGESTION	Sensación de quemazón. Dolor abdominal. Diarrea. Náuseas. Vómitos. Shock o colapso.	No comer, ni beber, ni fumar durante el trabajo.	Enjuagar la boca. Dar a beber agua abundante. NO provocar el vómito. Proporcionar asistencia médica.

DERRAMES Y FUGAS	ALMACENAMIENTO	ENVASADO Y ETIQUETADO

Barrer la sustancia derramada e introducirla en un recipiente tapado. Recoger cuidadosamente el residuo, trasladarlo a continuación a un lugar seguro. NO absorber en serrín u otros absorbentes combustibles. (Protección personal adicional: traje de protección química, incluyendo equipo autónomo de respiración.) NO permitir que este producto químico se incorpore al ambiente.	Separado de sustancias combustibles y reductoras, metales en forma de polvo . Bien cerrado.	NU (transporte): Ver pictograma en cabecera Clasificación de Peligros NU: 5.1 Grupo de Envasado NU: II CE: símbolo O símbolo Xn símbolo N R: 8-22-50/53 S: 2-60-61 

VEASE AL DORSO INFORMACION IMPORTANTE

ICSC: 0672 Preparada en el Contexto de Cooperación entre el IPCS y la Comisión Europea © CE, IPCS, 2003

Fichas Internacionales de Seguridad Química

PERMANGANATO DE POTASIO

ICSC: 0672

DATOS IMPORTANTES

ESTADO FISICO: ASPECTO:
Cristales púrpura oscuro .

PELIGROS FISICOS:

PELIGROS QUIMICOS:
La sustancia se descompone al calentarla intensamente, produciendo gases tóxicos y humos irritantes . La sustancia es un oxidante fuerte y reacciona con materiales combustibles y reductores, causando peligro de incendio o explosión. Reacciona violentamente con metales en forma de polvo , originando peligro de incendio.

LIMITES DE EXPOSICION:
TLV: (como Mn) 0.2 mg/m³, como TWA; (ACGIH 2003).
MAK: (como Mn) 0.5 mg/m³ I;
Riesgo para el embarazo: grupo C; Categoría de limitación de pico: 1;
(DFG 2003).

VIAS DE EXPOSICION:
La sustancia se puede absorber por inhalación del polvo y por ingestión .

RIESGO DE INHALACION:
La evaporación a 20°C es despreciable; sin embargo, se puede alcanzar rápidamente una concentración nociva de partículas en el aire cuando se dispersa.

EFECTOS DE EXPOSICION DE CORTA DURACION:
La sustancia es corrosiva para los ojos, la piel y el tracto respiratorio. Corrosiva por ingestión. La inhalación del polvo de esta sustancia puede originar edema pulmonar (véanse Notas). Los efectos pueden aparecer de forma no inmediata. Se recomienda vigilancia médica.

EFECTOS DE EXPOSICION PROLONGADA O REPETIDA:
La sustancia puede afectar al pulmón, dando lugar a bronquitis y neumonía .

PROPIEDADES FISICAS	Se descompone por debajo del punto de fusión a 240°C Densidad: 2.7g/cm³	Solubilidad en agua, g/100 ml a 20°C: 6.4 Presión de vapor, Pa a 20°C: despreciable
DATOS AMBIENTALES	La sustancia es muy tóxica para los organismos acuáticos.	

NOTAS

Enjuagar la ropa contaminada con agua abundante, (peligro de incendio). Los síntomas del edema pulmonar no se ponen de manifiesto, a menudo, hasta pasadas algunas horas y se agravan por el esfuerzo físico. Reposo y vigilancia médica son, por ello, imprescindibles.

Ficha de emergencia de transporte (Transport Emergency Card): TEC (R)-51G02-I+II+III

INFORMACION ADICIONAL