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Content

Biodegradation of phenol at high organic loads in a newly configured reactor using an aerobic-anaerobic reactor design with UASB type at low dissolved oxygen rates

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Abstract

Among the aromatic compounds present in industrial effluents, phenols are considered as priority contaminants. Due to its great use, has caused, that are present in: air, food, drinking water and natural bodies of water. Industries such as: chemistry, pharmaceutical, paper, etc., discharge wastewater with concentrations between 35 y 400 mg/L of phenol. While the discharges from Mexican refineries show concentrations of 30,000 mg/L. Their effects are adverse in the short, medium and long term in human health and aquatic life, when these effluents without receiving any previous treatment, are discharged to the natural bodies of water.The objective of this work was to evaluate the performance of a reactor of new aerobic-anaerobic configuration at low rates of dissolved oxygen on the phenol biodegradation efficiency of an industrial effluent, varying the organic load and the hydraulic retention time (HRT) to 30±0.5ºC and dissolved oxygen 1.54±0.7 mg/L, without pH control, or recirculation. The results showed that the best rate of phenol removal (47%), was achieved with an organic load of 57.7±1.3 Kg COD/m^{3}·d and HRT of 0.5 days (experiment II). While the COD removal (67%), was achieved at lower organic load (36.9±0.68 Kg COD/m^{3}·d) and HRT of 0.75 days (experiment III).

Anaerobic-aerobic, Hybrid reactor, Phenols, Toxicity, Biodegradation

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Introduction

The presence of phenols in the environment is a result of both natural and anthropogenic actions contribution mainly agricultural and industrial character. The production processes of industries; pharmaceutical, perfumery, explosives, phenolic resins, plastics, textiles, oil, dyes, leather, paper, coking plants, distilleries tar and pesticides, among others, expelled about 26.3% of phenols air, 73.3% in their wastewater discharges and about 0.4% in soil and aquatic sediments (ATSDR, 2016). Discharges of wastewater from the chemical, pharmaceutical, paper, foundry, etc., provide concentrations between 35 and 400 mg/L of phenol (Lepik and Tenno, 2011; Pramparo et al., 2012). However, the presence of phenol in wastewater has been reported with concentrations up to 10,000 mg/L (Krastanov et al., 2013). And in extreme cases, with concentrations of the order of 30,000 until 80,000 mg/L in effluents from the petrochemical industry (Terreros et al., 2016). Most countries specify a maximum allowable concentration of phenol in wastewater to be less than 1 ppm (Maleki et al., 2005).

The exposure of phenol and its derivative compounds to human and animals causes liver and kidney damage, central nervous system impairment, diarrhea, and excretion of dark urine (Olujimi et al., 2010). Therefore, it is necessary to develop methods that allow one to detect, quantify and remove phenol from wastewater (Mahvi, 2008). Generating a major problem for its elimination, which because it is a compound of benzene origin, is highly toxic and recalcitrant. The problem is exacerbated when in addition to phenol, effluents contain other compounds of similar toxicity, such as formaldehyde.

A situation that arises when it comes to effluents from resin processing, further complicating its purification (Ortega-Méndez et al., 2015).

A wide variety of microorganisms are known to be capable of metabolising many of the organic pollutants or chemicals generated and discharged (Badia-Fabegrat et al., 2014). Metabolic processes are governed by the action of enzymes. Enzymes are specific for each type of reaction. The three major classes of these energy-yielding processes are: aerobic respiration, anaerobic respiration and fermentation. Many microbes are capable of completely metabolising or mineralising different environmental organic pollutants like phenol under aerobic and/or anaerobic conditions and the Pseudomonas species have demonstrated the ability to do this effectively, as Pseudomonas spp than tolerate concentrations of 10 to 25 g/L of phenol as Alcaligenes cepa TW1 (Essam et al., 2010), Rhodococcus opacus (Matera et al., 2010), etc.

The wide variety of microorganisms that can aerobically degrade phenol include pure bacterial cultures such as: Acinebacter calcoaceticus, Alcaligenes eutrophus (Leonard and Lindley, 1998), Bacillus stearothermophilus, Pseudomonas cepacia G4 also known as Burkholderia cepacia G4, Pseudomonas picketti, Pseudomonas putida are also capable of degrading phenol. Yeasts as Candida tropicalis which uses phenol under aerobic conditions as the only source of carbon and energy, with a potential for degradation up to 1700 mg/L (Yang et al., 2005), Rhodotorula rubra, Trichosporon cutaneum and algae as Ochromonas dánica (Komarkova et al., 2003).

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Amongst all the microorganisms listed as good degraders of phenol, the pure culture of Pseudomonads are the most utilized purposely for metabolic pathway studies and their ability to utilize or degrade many other aromatic compounds. In Pseudomonads, many of its induced enzymes are non-specific and its metabolic pathway contains a high degree of convergence, allow for the efficient utilization of a wide range of growth substrates while the non specificity of the induced enzymes allows for the simultaneous utilization of several similar substrates without an excess of redundant genetic coding for enzyme induction (Selesi et al., 2010). Other techniques include the encapsulation of microorganisms as an alternative to protect against the toxicity of effluents with phenol (Martínez-Trujillo et al., 2012). Its incorporation of free form in the treatment systems, as it is known, presents certain limitations due to the inherent toxicity of this type of contaminant, as well as to the competition between the native populations and the exogenous (Fantroussi and Agathos, 2005). To resolve this limitation, immobilized microorganisms have been used, with immobilization the cells are given a protection against the toxic effect of the toxic substances such as phenol present in the effluent to be treated and predation by other populations (Martínez-Trujillo et al., 2012). What has allowed to increase the overall rate of biodegradation, due to the high cellular densities reached, in addition to increasing the stability and tolerance of microorganisms to toxic compounds (Aneez Ahamad et al., 2011).

Biological processes have been poorly studied because it has been demonstrated that the presence of 10 mg/L of phenol in wastewater causes inhibition of microorganisms, consequently a low removal efficiency.

However, the study of the biodegradation of phenolic compounds via aerobics has shown that there is a common metabolic pathway for this type of compound and even for those not so close to the family of phenolic compounds as biphenyls. Under anoxic respiration conditions (anaerobic digestion), it uses different electron acceptors such as nitrate, sulfate, CO2, among others. With the purpose of produce reduced compounds of nitrogen, sulfur, methane and carbon dioxide. (Shalaby, 2003).

Aerobic biodegradation of phenol.- In microbial degradation of phenol under aerobic conditions, the degradation is initiated by oxygenation in which the aromatic ring is initially monohydroxylated by a mono oxygenase phenol hydroxylase at a position ortho to the pre-existing hydroxyl group to form catechol. This is the main intermediate resulting from metabolism of phenol by different microbial strains. Depending on the type of strain, the catechol then undergoes a ring cleavage that can occur either at the ortho position thus initiating the ortho pathway that leads to the formation of succinyl Co-A and acetyl Co-A or at the meta position thus initiating the meta pathway that leads to the formation of pyruvate and acetaldehyde. Leonard and Lindley (1998), described the biodegradation or metabolism of phenol by Pseudomonas putida, Pseudomonas cepacia, Pseudomonas picketti and Alcaligened eutrophus respectively via the meta cleavage pathway, while Paller et al. (1995) described the biodegradation of phenol by Trichosporon cutaneum, Rhodotorula rubura and Acinetobacter calcoacetium respectively via the ortho cleavage pathway.

The meta pathway for the biodegradation of phenol as presented by Nelson et al. (1987).

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The mono oxygenase phenol hydroxylase of the Trichosporon cutaneum, Pseudomonas pickett, Bacillus stearo thermo phylus BR219 and some species of acinetobacter and alcaligenes are monocomponent flavoproteins (Kim et al., 2002), while the mono oxygenase phenol hydroxylase of pseudomonas CF-600 and Acinetobacter radioresistens (Shingler et al., 1998) are multicomponent proteins. Multicomponent aromatic mono oxygenases contain at least two components. The former is an oligomeric protein while the latter is a monomeric iron transfer flavoprotein. Infact, the three-component toluene dioxygenase (TDO) from Pseudomonas putida uses dioxygenation followed by water elimination to convert phenol to catechol (Spain et al., 1989).

Anaerobic biodegradation of phenol .- Phenol can also be degraded in the absence of oxygen and it is less advanced than the aerobic process. It is based on the analogy with the anaerobic benzoate pathway proposed for Paracoccus denitrificansin (Williams and Evans, 1975). In this pathway phenol is carboxylated in the para position to 4 hydroxybenzoate which is the first step in the anaerobic pathway. Here the enzyme involved is the 4-hydroxy benezoate carboxylase. The anaerobic degradation of several other aromatic compounds has been shown to include a carboxylation reaction. Carboxylation of the aromatic ring in para position to the hydroxyl group of o-cresol resulting in 3-methyl 4-hydroxybenzoate has been reported for a denitrifying Paracoccus like organisms, as well as methogenic consortium was later shown to travel a varity of phenolic compounds including o-cresol, catechol and ortho halogenated phenols via para carboxylation followed by dehydroxylation.

The organisms capable of degrading phenol under anaerobic conditions were Thauera aromatica and Desulphobacterium phenolicum.

Aerobic or anaerobic studies for phenol biodegradation address the use of synthetic waste water and in some cases, industrial wastewater with hydraulic retention times (HRT) greater than 1 day, high rates of dissolved oxygen, low organic loads and in some cases, the use of co-substrates such as glucose (Godjevargova, 2003; Suarez et al., 2007; Bajaj, 2008; Farooqi, 2008; Donoso-Bravo, 2009; Tavares et al., 2009; Chérif, 2011; Almasi, 2012; Anushuya Ramakrishnan, 2013; Rosenkranz, 2013, Pradeep, 2015). His biodegradation by this type of processes, involves many factors such as; Organic loading speed (Liu et al., 2003a), temperature, pH, dissolved oxygen concentration, substrate concentration, dilution rate (Ba et al., 2014), thus as the acclimatization strategy (Terreros et al., 2016).

The objective of this work was to evaluate the performance of a reactor of new aerobic-anaerobic configuration at low rates of dissolved oxygen on the phenol biodegradation efficiency of an industrial effluent, varying the organic load and the hydraulic retention time (HRT) to 30±0.5oC, without pH control, or recirculation, taking advantage of the benefits of mixed microbial cultures. Through the acclimatization of biomass at a low organic load rate, with the aim of increasing over time its biodegradability at higher organic loading rates. The than is relevant and novel to have two microbial consortia in a single reactor, which in addition to being innovative, environmentally friendly, lowers the costs of treatment of this type of effluent, in relation to the technologies traditionally used.

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Materials and methods

Description of the UASB reactor

For the tests a hybrid reactor type UASB was used Upflow Anaerobic Sludge Blanket) at laboratory scale with design volume of 1.21L, useful volume of 1.04L, internal diameter of 4.5 cm and height of 53 cm (figure 1).

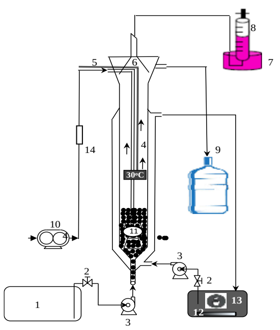

Figure 1 Description of the process. 1) Phenolic residual water, 2) Regulating valve, 3) Peristaltic pump, 4) Reactor UASB, 5) Temperature sensor, 6) Phase separation device, 7) Recipient of Saline solution pH 2, 8) Biogas measurement column, 9) Recipient of treated water, 10) Air pump, 11) Air conduction device, 12) thermostat, 13) Water container to 30±0.5oC, 14) Air flow meter

Inoculum.- The reactor UASB, was inoculated with 312 mL of sludge (total volume), of the which 94 mL correspond to aerobic sludge that was collected from an activated sludge reactor of the municipal wastewater treatment plant “Cerro de la Estrella”, of Mexico City, with a concentration of 12.7 g/L de TSS and 9.7 g/L of VSS. And 218 mL of anaerobic granular sludge from a reactor UASB of the Autonomous Metropolitan University Iztapalapa unit that treats the wastewater of the academic unit, with a concentration of 67.9 g/L de TSS, 35.7 g/L of VSS and specific methanogenic activity (SMA) of 0.11 LCH4/gVSS·d.

Feed medium (Influent).- During the first week of operation, mineral medium was used RAMM (Shelton and Tiedje, 1984) with sodium acetate as the carbon source for the development of the methanogenic conditions of anaerobic biomass. And a dilution rate of 2% of phenolic residual water to acclimatize the biomass against this toxic. From the second week and throughout the experimental period, the reactor was fed with phenolic residual water. Calculating from Equation C1V1 = C2V2, the volume of phenolic residual water required to prepare the feed according to the fraction v/v of the 25 and 40% based on the characteristics of the industrial wastewater samples provided (table 1).

Parameter	**Experiment**		
	I X±S	**II** X±S	**III** X±S
Fraction v/v	25%	40%	40%
COD (g/L)	17.84±0.025	27.7±0.44	27.8±0.3
Phenol (g/L)	3.37±0.04	5.34±0.06	5.34±0.02
pH	6.82±0.13	5.25±0.34	5.15±0.2
TS	0.68±0.2	0.3±0.19	0.26±0.15
VS	0.45±0.05	0.23±0.04	0.14±0.08

Table 1 General characteristics of industrial residual water with phenol (influent)

Characterization of wastewater and evaluation of reactor performance.- For the characterization of the industrial effluent and evaluation of reactor performance (analysis of the difference of parameters) between the mixture of phenolic fed water and treated, the following parameters were analyzed (COD, phenol, pH, TS and VS) using the following analytical techniques; Chemical oxygen demand (COD), total solids (TS) and volatile solids (VS) were determined according to the standard method (APHA, 2016).

The pH was evaluated by a potentiometer (Conductronic PC18). The phenol analysis was performed by the colorimetric method of 4-aminoantipyrine according to the Mexican standard (NMX-AA-050-SCFI-2001) using an equipment UV-VIS brand Perkin Elmer Spectrometer model Lambda XLS. The volume of biogas produced was quantified by inverted column in a vessel containing a saline solution at pH=2. Where, the volume of the displaced solution corresponded to the volume of biogas produced. The rate of dissolved oxygen supplied to the studied system was measured using a portable model YSI.

Operating conditions of the reactor.- For the operation of this type of reactor of new configuration, a device was used to separate both types of microbial consortium (aerobic-anaerobic) and to avoid their possible mixture. Feeding the reactor to continuous flow in the different runs in which the experiment was carried out (table 2), by means of a peristaltic pump. Furthermore, of a thermostat to maintain the working temperature of 30±0.5°C, and an air flow meter model "Dwyer", applying a hydraulic retention time (HRT) of 12 h, without pH control, agitation or recirculation.

Experiment	**I**	**II**	**III**
Fraction v/v of $RW_{Phenólic}$	25% X±S	40% X±S	40% X±S
Bv (kgCOD/m^{3}·d)	34.4±0.7	57.7±1.3	36.9±0.68
HRT (days)	0.5	0.5	0.75
Dissolved oxygen (mg/L)	1.54±0.7	1.54±0.7	1.54±0.7

Table 2 Operating conditions of the reactor

Results and Discussion

Characteristics of the treated phenolic residual water (effluent).- Before addressing the analysis of the results, it is presented in the table 3, the results of the averages of the main parameters evaluated to the treated wastewater samples taken throughout the experiment, to evaluate the performance of the newly configured reactor, on the phenol biodegradation rate of the industrial residual water. And there is a significant dispersion in the data, due to the variability that occurs during the treatment of phenolic industrial effluent from the polymer resins industry.

Parameter	**Experiment**		
	I X±S	**II** X±S	**III** X±S
COD (g/L)	7.42±0.36	17.6±0.6	9.27±1.2
Phenol (g/L)	2.56±0.18	2.84±0.47	3.18±0.34
pH	6.98±0.14	6.59±0.18	6.66±0.12
TS	0.73±0.25	0.29±0.14	0.26±0.15
VS	0.54±0.15	0.19±0.1	0.17±0.1

Table 3 General characteristics of treated wastewater (effluent)

In the figure 1, the behavior of pH during the development of the experiment is shown. The clear rhombuses represent the pH in the influent and the dark rhombuses, the pH of the effluent. And you can say in general terms, that the performance of the biological reactor throughout the experiment was adequate.

Despite having presented a variation pH in the 2 last samples of industrial phenolic residual water with which the hybrid system was fed during the experiments II y III, with an average pH value of 5.2±0.2, did not affect the metabolic activity of both bacterial consortia of the experimental system. The anaerobic digestion of organic matter is carried out in a range of pH between 6.2 and 7.8, with an optimum between 7 and 7.2 (Metcalf and Eddy, 2016).

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Variations of pH, affect the enzymatic activity of microorganisms by changes in the state of the ionizable groups, which causes alteration of the non-ionizable components of the system such as denaturation of the protein structure of the enzymes. High pH values favor the formation of free ammonia, inhibitor of the methanogenic phase which causes an imbalance between the production and the consumption of volatile fatty acids by accumulation of these, acidifying the reactor (Zeeman and Sanders, 2001). While extreme values of pH (less than 3 or greater than 9) may be inhibitory to the growth of microorganisms involved in phenol biodegradation (El-Naas et al., 2009). In this context, the behavior of pH in the reactor allowed the study, object of this research work, to be carried out adequately.

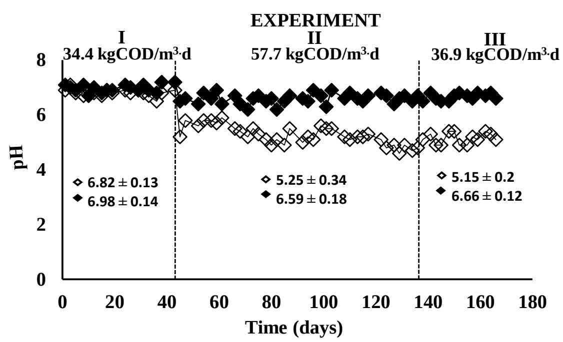

Figure 1 Variation of pH with time

In the figure 2, is shown the profile of volatile solids (VS). The clear rhombuses represent the VS in the influent and the dark rhombuses, the SV in the effluent. Most studies of phenol degradation and related compounds have been focused on microbial consortia that have previously been acclimated to the toxic compounds under study (Antizar-Ladislao and Galil, 2004). However, to date there is very little information on the dynamics and degree of adaptation achieved according to the strategy used to acclimate the microbial consortium to phenol.

In this context, during the development of the research, once industrial residual water was fed with a phenol concentration of 3.37±0.04 g/L, with organic load of 34.4±0.7 KgCOD/m3.d (experiment I), there is a slight biomass loss from the reactor. In the literature it is mentioned that due to the bactericidal effect of phenol, based on the ability of the compound to dissociate within the cells, it can cause the cytoplasmic membrane functions to be interrupted, which probably caused the death of some of the anaerobic cells (Tay et al., 2005), and consequently, the presence of solids in the reactor effluent. In addition, at high organic loading rates, a loss of cell integrity may occur and consequently, the disintegration of the granular structure (Quarmby and Forster, 1995).

Which apparently did not affect the aerobic consortium as in the case of aerobic granules, these may be formed in a wide range of organic loading, of 2.5 to 15 KgCOD/m3.d (Moy et al., 2002). Increasing the size of the aerobic granules of 1.6 to 1.9 mm with organic loads of 3 to 9 KgCOD/m3.d (Liu et al., 2003a). However, for the following runs, once the biomass of the new configuration hybrid reactor was adapted to the presence of phenol (Tay et al., 2005; Marrot et al., 2006; Vacca et al., 2008; Farooqi et al., 2008), presents stable conditions during the biodegradation of phenol, which allowed to reach that volatile solids in the effluent of the reactor, were in average of 0.19±0.1 and 0.17±0.1 g/L respectively (experiments II and III). Therefore, in addition to the factors involved during the biodegradation of phenol, in biological processes such as: temperature, pH, dissolved oxygen content, substrate concentration, among others (Nair, 2008; Agarry, 2008; Trigo, 2009), as well as organic loading (Moy et al., 2002; Liu et al., 2003a). It is very important to have a good biomass acclimatization strategy (Terreros et al., 2016).

To achieve the maximum rate of biodegradation of phenol present in an industrial effluent, in such a way, that the biomass does not present any type of inhibition or affectation of its metabolism and much less, to cause its cell death, by exposure to this type of toxic compounds (Luo, 2009).

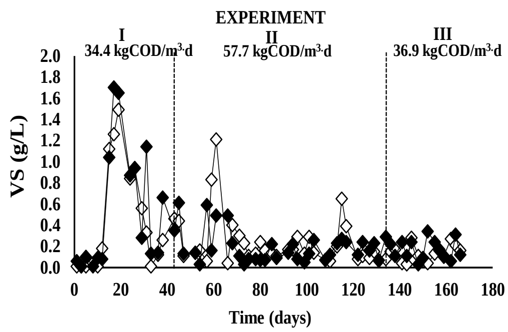

Figure 2 Variation of volatile solids during the biodegradation of phenol

The figure 3 shows the removal efficiency of chemical oxygen demand (COD) during the development of the experiment at different fractions v/v of residual water with phenol: 25 and 40% (table 2). The clear rhombuses represent the COD in the influent and the dark rhombuses, the COD remaining in the reactor effluent. And it is appreciated that once the reactor was fed with phenolic residual water with an organic load of 34.4±0.7 Kg COD/m3.d (experiment I) to 0.5 days of hydraulic retention time (HRT), Efficiency of removal of COD, from the 57%.

However, with the increase of the organic load in 57.7±1.3 Kg COD/m3.d during the experiment II, the efficiency of COD removal decreased significantly in one 29% on day 101 of operation. And it is observed that to the extent that the biomass acclimatizes to the presence of the phenol, the removal efficiency, is gradually recovered until reaching a 49%.

However, by varying both the organic load in 36.9±0.6 Kg COD/m3.d (organic load similar to the experiment I), as the hydraulic retention time in 0.75 days, during the experiment III, an improvement on the COD removal rate was observed in 67% based on the removal rate achieved during the experiment I.

In the literature it is mentioned that both aerobic and anaerobic granules can be formed over a wide range of organic charge rates ranging from 2.5 a 15 Kg COD/m3.d (Moy et al., 2002; Liu et al., 2003a), with an increase in size from 1.6 to 1.9 mm with organic loads over a range of 3 a 9 Kg COD/m3.d (Liu et al., 2003b), that in addition to factors such as pH, temperature, etc. that influence reactor performance during phenol degradation, it is important to acclimate to biomass (Terreros et al., 2016) to achieve the best results in order to avoid partial loss of its integrity, and consequently the disintegration of its granular structure, given the toxic effect of phenol, which causes inhibition of microbial growth according to what has been reported in other studies (Chen et al., 2008; Liu et al., 2008).

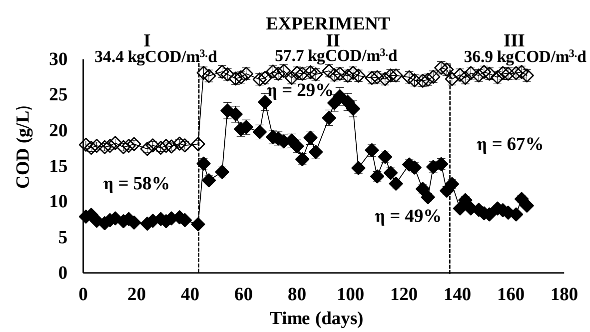

Figure 3 Variation of COD concentration with time

In the figure 4, is shown the rate of phenol biodegradation under the tested operating conditions (table 2). The clear rhombuses represent the phenol concentration in the influent and the dark rhombuses, the phenol concentration remaining in the reactor effluent.

And it is observed that the best rate of phenol removal was achieved during the second run, with a fraction v/v phenolic residual water from the 40%, organic load of 57.7±1.3 Kg COD/m3.d, dissolved oxygen rate of 1.54±0.7 mg/L and 0.5 days of HRT.

And it is observed during the last run of the experiment, in which the reactor was fed with a fraction v/v similar to that of the second experiment (fraction v/v of 40%), but lower organic load (36.9±0.8 Kg COD/m3.d) similar to the experiment I. A higher phenol biodegradation rate (40%) with greater HRT of 0.75 days. Compared with the phenol biodegradation rate achieved during the first run. These results show that in order to achieve an adequate rate of biodegradation of phenol present in industrial wastewater by biological processes, it is necessary to make dilutions (Ba et al., 2014).

Since in the measure in which it increases its concentration, decreases the rate of phenol biodegradation by microorganisms. In this context, the reactor performed adequately in the study, without affecting the biomass at the phenol concentrations of the wastewater studied. Although at concentrations of phenol of more than 1300 mg/L, it causes an inhibitory effect (decrease of the metabolic activity of the biomass) and even, can lead to the total loss of its microbial activity (Busca et al., 2008).

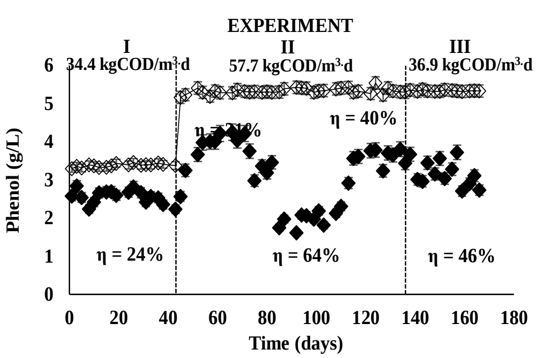

Figure 4 Variation of phenol concentration with time

In the figure 5, it is noted that the measure in that the organic load increases of 34.4±0.7 to 57.7±1.3 KgCOD/m3.d to 0.5 days of HRT, the rate of biogas production, decreases significantly from 19.2±1.5 mL (experiment I) to 5.4±1.1 mL (experiment II). And it is note that increasing the HRT 0.5 to 0.75 days during the last experiment, a slight reduction occurs place in biogas production, probably due to the concentration and exposure time of the biomass with phenol, causing that the metabolic activity of the anaerobic bacteria to be more sensitive to this toxic compound, present less methanogenic activity and, consequently, less production of biogas (Busca et al., 2008).

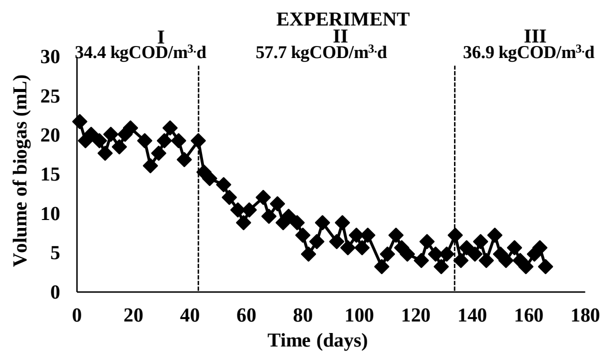

Figure 5 Biogas production with time

Conclusions

The strategy used to acclimate the aerobic and anaerobic microbial consortium used as reactor inoculum to study the biodegradation of phenol present in a real industrial effluent was the key factor in achieving the objective set out in this study.

With the results obtained, it has been demonstrated that it is possible to treat phenolic industrial effluents by the use of reactors of new configuration using an aerobic-anaerobic reactor design type UASB, at low rates of dissolved oxygen.

The use of this new design of hybrid reactor of new configuration, Is an excellent alternative for the solution of real problems of environmental pollution, by discharge of industrial effluents with phenol, that besides being new, environmental friendly, is robust, by its capacity of biodegradation of phenol, at high rates of organic load, in relation to the technologies traditionally employed. With the use of this biotechnology, it can enhance the design and Construction of a new type of wastewater treatment plant With high concentration of toxic compounds as phenol, which in addition to lowering its construction costs, operation and maintenance, the surface for its construction it is less, significantly reducing investment costs.

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Electrical characteristics of a CNTFET and an SB-CNTFET through compact modelling for different chiralities

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Abstract

Objectives, methodology: One of the most important aspects noticed about CNTs is the study of the physics of the one-dimensional (1D) systems in electronics. It is important that the CNFET model, takes into account not only the physic related to this 1D semiconductor device, but also that it allows us to simulate the device behaviour in environments such VHDL or H-SPICE. In this work simulations were made through a generic compact model for two kinds of CNTFETS: a C-CNTFET and an SB-CNTFET. This model includes effects such as the Shottky Barrier created in CNT/metal contacts and the temperature, which may provide I-V characteristic curves more accurate approximating to the real behaviour of a CNFET. Contribution: MOSFET technology made possible an impressive progress in VLSI, given its capability to be scaled and still has also very good performance, however it has been observed that in the nanometric range this kind of devices shows unwanted characteristics, better known as SCEs (short channel effects). One of the most unwanted consequences of these SCEs is that the gate terminal loses some of its control over the transport characteristics. Other ones are the not-controlled quantum mechanical effects, principally tunnelling effects.Some alternatives have emerged to avoid these unwanted effects; one of the most outstanding is that involves carbon nanotubes (CNT). In this work we present the electrical characteristics I-V of a C-CNTFET and an SB-CNTFET, such characteristics were obtained using the compact modelling and considering a SWCNT, with semiconductive behaviour. We use three different chirality indexes (13, 0), (19, 0), (38, 0), which give three different diameters 1.02 nm, 1.48 nm y 3 nm, and energy gaps of 0.8370 eV, 0.5727 eV and 0.2863 eV respectively, such chirality values led to some interesting differences in the I-V response.

CNT, C-CNFET, SB-CNTFET, electrical characteristics, compact modelling

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Introduction

This work presents I-V curves of the C-CNTFET and the SB-CNTFET, based on the compact modelling, this model provides a current equation, which is obtained with the assumption that the transport in the CNT is ballistic, in which case is ignored the dispersion effects due to the interaction between electrons and lattice vibrations and defects. This model also includes the height barrier modulation in the source (S) and drain (D) regions, which allows making a comparison between the well-known metal-oxide-semiconductor field effect transistor (MOSFET) and CNTFET, this due to the MOSFET is a device that can modulate the current flow in its channel by modelling the potentials applied on its terminals, gate, source and drain.

While manufacturing a C-CNTFET (Conventional Carbon Nanotube Field Effect Transistor) needs a major technological investment, it is more affordable in these terms to achieve the manufacturing of an SB-CNTFET (Shottky Barrier Carbon Nanotube Field Effect Transistor), so it became important to take into account how including an SB which would change the I-V response.
Normally temperature turns out to be an important factor in semiconductor devices, nevertheless in the case of CNT devices it does not show the same influence, however temperature will always be a factor to take into account in terms of the development of the device.

C-CNTFET

Compact modelling of CNTFET (C-CNTFET) of A. Raychowdhury (Raychowdhury, 2004) it is retaken to investigate the electrical characteristics of a C-CNTFET, this device has an operational mode that resembles to the MOSFET one, in the sense that it is applied the principle of height barrier modulation through the modulation of the potential applied to the gate terminal (V_G).

It is due to its own geometry, that C-CNFET allows this performance, in this geometry the CNT gets wrapped by an oxide of high-κ (dielectric constant), which in a way represents a barrier for tunnelling phenomena, after this material another wrapped corresponding to gate material cover the CNT. Figure 1 shows a squematic arrangement of the CNTFET structure exhibiting the source (S), CNT channel and drain (D), such components are supported by a thin oxide film (SiO_2) followed by a silicon semiconductor substrate type P++.

The portions corresponding to source and drain, are segments of CNT highly doped, both of them will contribute to the flow of current, as it can be seen on current equation below.

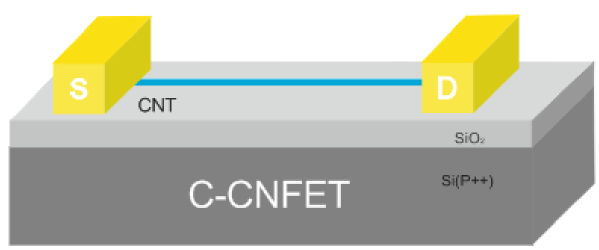

Figure 1 C-CNFET arrangement

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Current equation

Current equation is derived under the assumption that there is a ballistic transport in the CNT, so in this case is possible to calculate the electrical current which can be derivated from Landauer formula, to stablish that such current is as follows (Raychowdhury, 2004)

$$I_{ds} = \frac{4qk_BT}{h}\sum_{p=1}^{p=n}\{\ln\left(1+e^{\xi_S}\right) - \ln(1+e^{\xi_D})\} \quad (1)$$

where q is the charge of electron and p indicates the number of sub-bands that contributes to this value of current, besides k_B is the Boltzmann constant, $T(K)$ the absolute temperature and h the Planck constant. The parameters ξ_S and ξ_D are determined as

$$\xi_S = \frac{-\Delta p + q(V_{CNT} - V_S)}{k_BT}, \quad (2)$$

$$\xi_D = \frac{-\Delta p + q(V_{CNT} - V_D)}{k_BT}. \quad (3)$$

(2) and (3) are source and drain contributions, and they fill the +k and –k states, which their difference provides the value of V_{DS}, additionally we have that

$$\Delta p = \Delta_1 \frac{6p-3-(-1)^p}{4}, \quad (4)$$

$$\Delta_1 = \frac{0.45}{d} = \frac{E_g}{2}, \quad (5)$$

where the Δp is the energy of the bottom of the p sub-band and Δ_1 is the bottom of the conduction band, d is the CNT diameter and Eg its energy gap chosen as $0.45eV$ according to this model.

Surface potential

Compact modelling considers the value of the potential in the channel using Poisson equation for getting the next consideration

$$V_{CNT} = V_{GS} \text{ for } V_{GS} < \Delta_{1,} \quad (6)$$

$$V_{CNT} = V_{GS} - \alpha(V_{GS} - \Delta_1) \text{ for } V_{GS} \geq \Delta_{1.}$$

Although it is a valid adjustment one more precise would be given by the next equation (Marki, 2013)

$$V_{CNT} = V_{GS} - 0.5\left\{\alpha(V_{GS} - \Delta_1) + \sqrt{\left(\alpha(V_{GS} - \Delta_1)\right)^2 + 4\varepsilon^2}\right\}. \quad (7)$$

The modulation of V_{CNT} potential is given by the modulation of V_{GS}, due to the presence of charge in the channel.

SB-CNTFET

For these SB transistors, the SB appears at the interfaces between the semiconducting nanotubes and the metallic leads, i.e. i) the work function of the metal electrodes is higher than that of the nanotubes and/or ii) when the nanotube is supposed to behave as a p-type semiconductor.
As in the C-CNTFET, the principle of functioning of an SB-CNTFET is similar to the MOSFET, this is because gate potential allows decreasing or increasing the height barrier, but one main difference is that the width barrier is modulated by drain bias, the other main difference is the ambipolar I-V response, this is consider by the fact that there is matching contributions of electrons and holes (Marki, 2014).

The approximation in this case came from solving 1-D modified Poisson equation for the channel potential, in order to calculate the effective SB height, which can be expressed as

$$\phi_{SB}{}^{eff} = (\phi_{SB} - V_{CNT})exp(-d_{tunnel}/\lambda) + V_{CNT}. \quad (8)$$

So the current equation is modified like this

$$I_{DS} = \frac{4qk_BT}{h}\sum_{p=1}^{p=n}\left\{ln\left(1 + exp\frac{qV_S+\phi_{SB}{}^{eff}-sbbd_p}{K_BT}\right) - ln\left(1 + exp\frac{qV_D+\phi_{SB}{}^{eff}-sbbd_p}{K_BT}\right)\right\}. \quad (9)$$

For a channel length larger than screening length V_D must be consider $-V_D$ (Knoch, 2008).

Temperature effect

In order to include the temperature effect in the current equation it is useful to consider the temperature dependence of the band gap of semiconducting single-wall carbon nanotube, this value is derived from the direct evaluation of electron-phonon coupling within a "frozen-phonon". A useful model relation Eg (T) of semiconducting SWNTs in the temperature range of T<400 K is that as a two phonon Viña model (Capaz, 2005) which gives the following equation:

$$\Delta E_g(T) = \frac{\alpha_1\Theta_1}{e^{\Theta_1/T}-1} + \frac{\alpha_2\Theta_2}{e^{\Theta_2/T}-1}, \text{ (eV)} \quad (10)$$

Θ_1 and Θ_2 are effective temperatures for the two "average phonons", these parameters have a direct relation with the SWNT diameter and chirality:

$$\Theta_1 = \frac{A}{d^2}, \quad (11)$$

where $d = \sqrt{n^2 + m^2 + nm}$, and

$$\Theta_2 = \Theta_2{}^{\infty} + \frac{f_{\Theta_2}(\xi)}{d}, \quad (12)$$

$$\alpha_2 = \frac{1}{d}\left(B + \frac{f_{\alpha_2}(\xi)}{d}\right), \quad (13)$$

$$\alpha_1 = \alpha_1{}^0 + f_{\alpha_1}(\xi)d. \quad (14)$$

It is possible to introduce this effect in the current equation by modifying (2) and (3) as it follows:

$$\xi_S = \frac{-E_T+q(V_{CNT}-V_S)}{k_BT}, \quad (15)$$

$$\xi_D = \frac{-E_T+q(V_{CNT}-V_D)}{k_BT}, \quad (16)$$

where $E_T = E_0 + \Delta E_g(T)$ and $E_0 = \frac{2a_{cc}|t|}{d}$, $a_{cc} = 1.42$Å and $t = -3eV$.

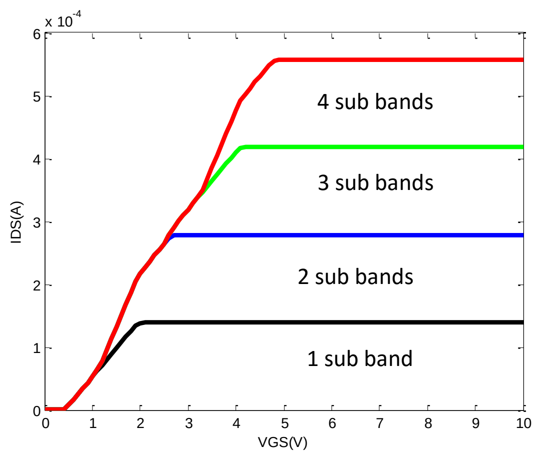
As it was mentioned above the compact modelling allows including many different factors that can modify the electric response in this type of devices, so in this work it is included the temperature effect as well as the SB effect in the current equation as it is introduced in the following equations

$$\xi_S = \frac{-E_T+qV_S+\phi_{SB}{}^{eff}}{k_BT}, \quad (17)$$

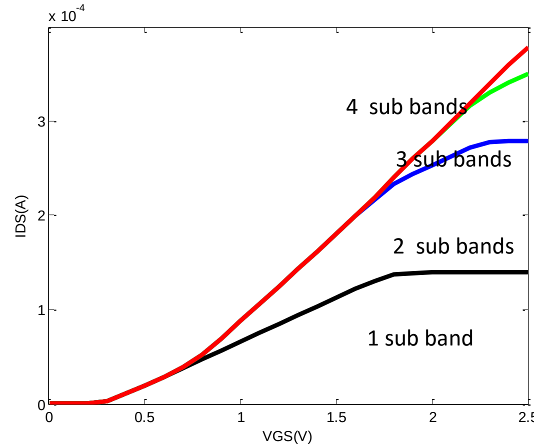
$$\xi_D = \frac{-E_T+qV_D+\phi_{SB}{}^{eff}}{k_BT}. \quad (18)$$

Results

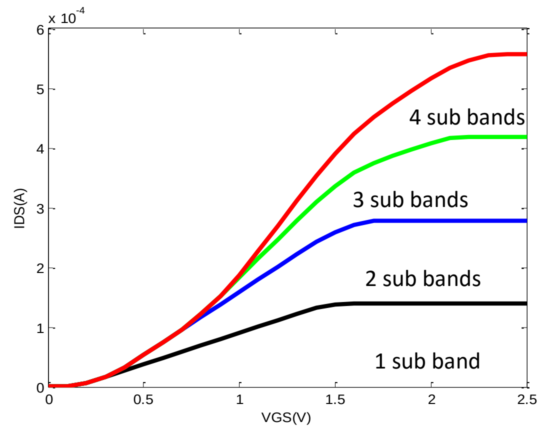
By virtue of the MOSFET and CNTFET work based on the height barrier modulation which depends on the value of gate potential V_G applied on the CNT, thus the energy level in the source and drain barriers decreases producing a major electron flow through the CNT channel. So the current value will depend on the number of carriers in the different sub-bands. The number of the sub-bands to take into account depends on the applied gate voltage (Raychowdhury, 2004). In graphic 1 it is possible to see how each band contributes to current value, so there is a minimum value of current curve just with 1 sub-band and the biggest value is obtained with the contribution of 4 sub-bands, however it is also possible to see how chirality affects the I-V response, and the one which exhibits better response corresponds to (38, 0) chirality.



a)



b)



c)

Graphic 1 I_{DS} vs V_{GS} V_{DS}= 0.9 V for a) (13, 0), b) (19, 0), c) (38, 0) chirality and the contribution of 4 sub-bands.

In the case of graphic 2 it is possible to see how the I-V response changes when, instead of ohmic contacts there is an SB contact formed in the interface CNT/metallic gate, in this case appears the ambipolar characteristic given for electrons and holes contribution. As it happens in C-CNTFET response, SB-CNTFET response is also very sensitive to changes in the chirality index, so in the case where the chirality index is the smallest one (13, 0), and the band gap has the value of 0.8370eV, the current value will be the biggest one, and it happens the opposite when the chirality index is the biggest one, (38, 0) and the band gap has the value of 0.2863 eV.

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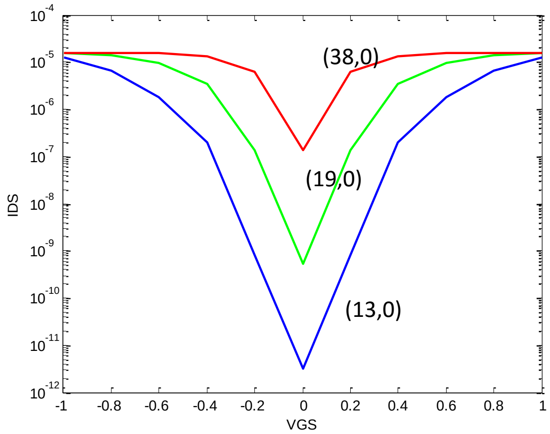
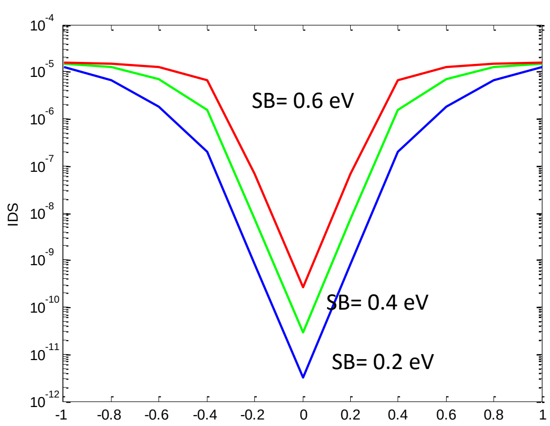


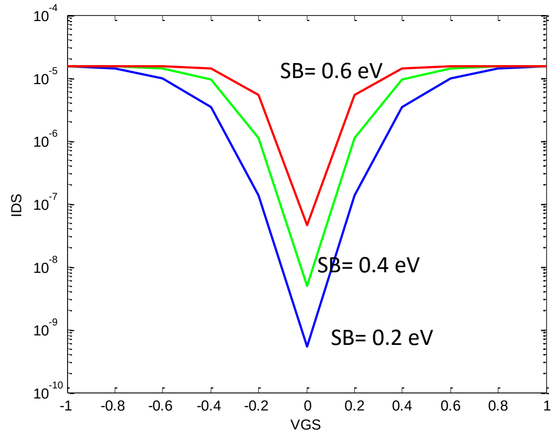
Graphic 2 I_{DS} vs V_{GS} for three different chiralities indexes (13, 0), (19, 0), (38, 0),V_{DS}=0.1V, SB=0.2 eV, d_{tunnel}= 4.125 nm, λ_S=3.29nm

It is predictable that by introducing different materials in contacts there SBs would have different values, so electrical response will also be different, and as it has seen before chirality index will also modified speed of response and current value. In graphic 3 it is possible to see two different aspects in each graphic, the first aspect is that when there are smaller SBs there will be a smaller current value, which is almost predictable because is only carriers with energies bigger than SB which would reach the channel (Marki, 2014).

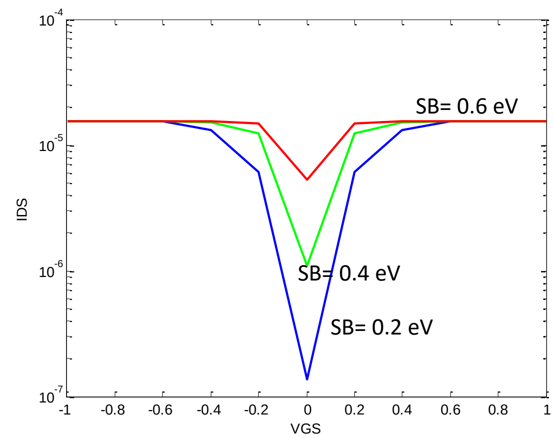
On the other hand, the current would also be decreased when chirality index has a bigger value.



a)



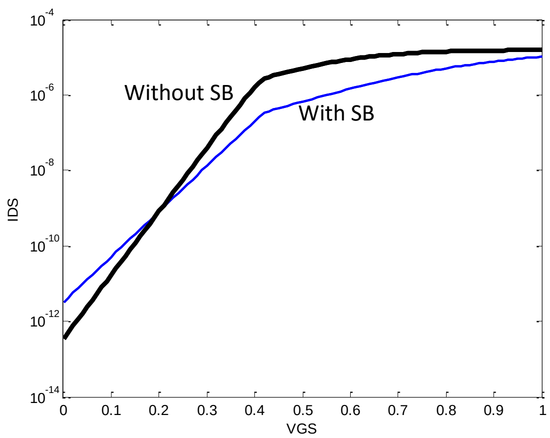
b)



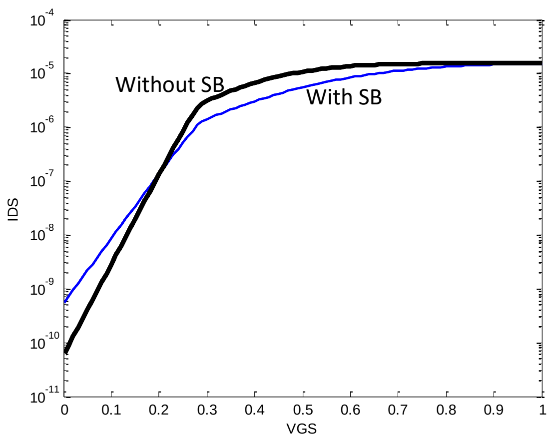
c)

Graphic 3 I_{DS} vs V_{GS}, V_{DS}=0.6V, for a) (13, 0), b) (19,0), c) (38,0) and three different SBs=0.2eV, 0.4 eV, 0.6eV, d_{tunnel}=4.125nm, λ_S=3.29 nm

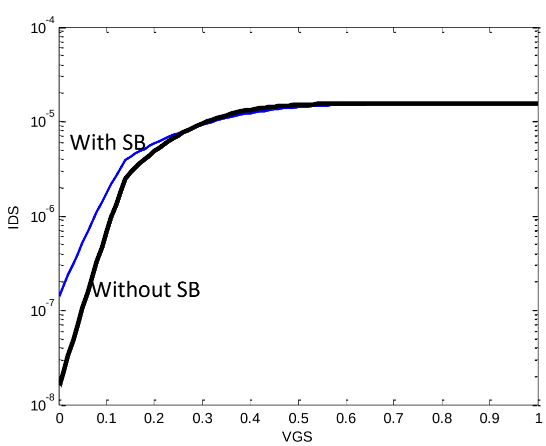
The next graphics, 4 and 5 allows comparing clearly how much the current value changes in both devices, with and without the SB effect, in all cases it is remarkable that the current diminishes with the presence of the SB effect as consequence of the obstruction of the flow carriers due to the barrier formed in the interface of the contact CNT/metal. It is more visible the differences in the case of I_{DS} as a function of V_{DS}. In both graphics, 4 and 5, there were used the following chiralities, a) (13, 0), b) (19, 0) and c) (38, 0).



a)

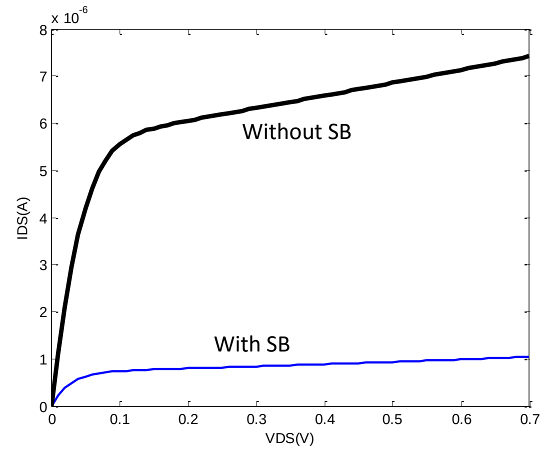


b)

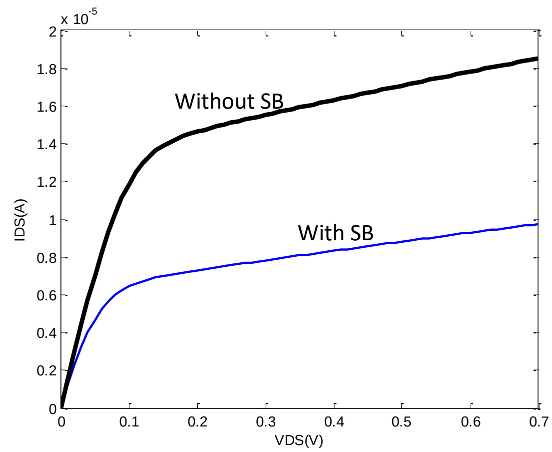


c)

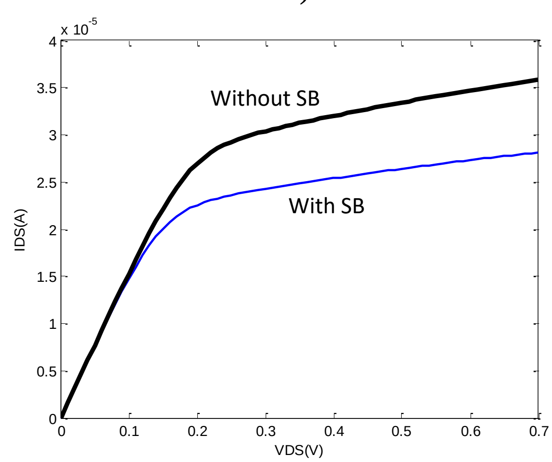
Graphic 4 I_{DS} vs V_{GS} with SB=0.2 eV and without SB, V_{DS}=0.1 V



a)



b)

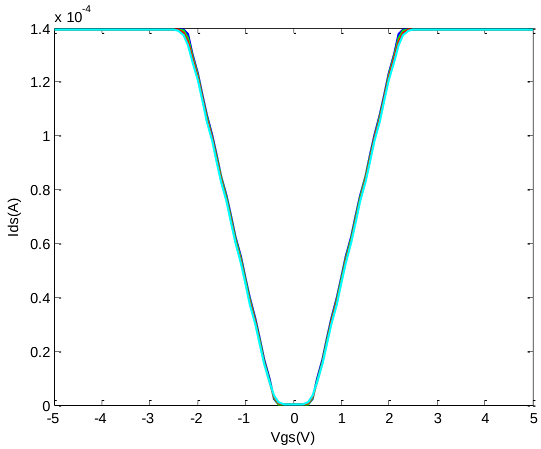


c)

Graphic 5 I_{DS} vs V_{DS} with SB=0.2 eV and without SB, V_{DS}=0.1 V

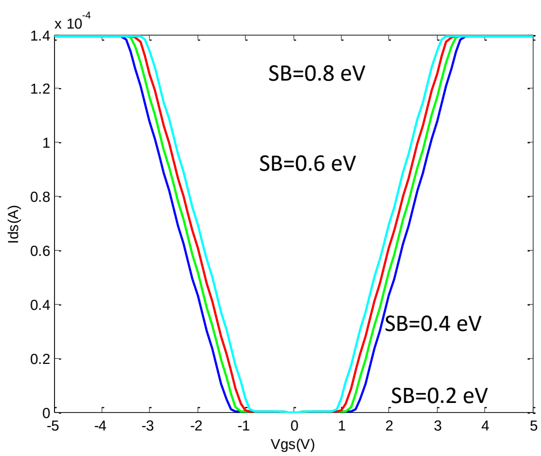
In graphics 6 and 7, temperature effect was introduced, as well as some variations for SBs values and the three different chiralities considered for previous simulations.

It is observable in graphic 6 that variations of temperature from 100 K- 400 K do not introduce significant changes in the I-V response, where we are also taking into account CNT/metal contact.



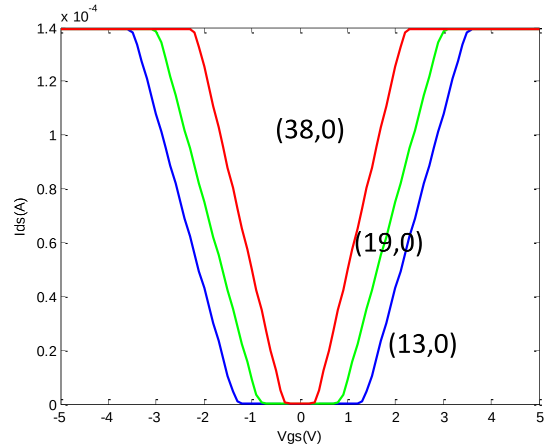
Graphic 6 I_{DS} vs V_{GS}, effect of temperature for T ranging from 100 K- 400 K, SB= 0.2eV, V_{DS}= 0.9 V, d_{tunnel}= 4.125nm, λ_S=3.29nm.

For graphic 7 variations in SBs values effectively show changes in current response, making it slower, in this simulation temperature was established in a value of 200 K.



Graphic 7 I_{DS} vs V_{GS}, V_{DS}=0.9V, SB=0.2 eV, 0.4eV, 0.6 eV, 0.8 eV, chirality index (38, 0), dt_{unnel}=4.125nm, λ_S=3.29nm, for 200 K

Finally, for graphic 8, temperature was settled in a value of 200 K, the SB has a value of 0.2 eV, in this case there was a variation in the value of chirality index, and it certainly modifies the response, for the biggest chirality index response turns out to be faster than for the smaller values.



Graphic 8 I_{DS} vs V_{GS}, V_{DS} = 0.9 V, three different chirality indexes (13, 0), (19, 0), (38, 0), SB = 0.2 eV, d_{tunnel} = 4.125nm λ_S=3.29nm.

Conclusions

It is outstanding how the geometrical characteristics have such a big influence on the electrical behaviour. In first place it is remarkable how diameter, which is directly related to chirality index, determines how fast it can be the I-V response, and also that finding the right diameter would provide a cleaner response.
Another important factor that makes the I-V response more sensitive it is taking into account the Shottky Barrier formed in CNT/metal contacts, the materials used in these contacts would determine the SB value, however the value of SB clearly diminishes the current value, this diminution is also determined by the value of the chirality index, which in appearance as big it is the diminution in current is lesser.

In the range of the temperature established for this work it is hard to notice a strong influence over current values, although it is possible to see again how an SB and chirality index give the bigger changes in value and fastness in current curves.

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Implementation of inventory levels for raw material at herramientas Stanley

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Abstract

Inventory management is a vital task within the supply chain. Most companies seek high inventory turnover as this could indicate effectively pulling in product sales. This project is focused on establishing efficient inventory levels and main-taining the company's competitiveness within the market. Herramientas Stanley (HS) manufactures demolition tools. Due to fluctuation in customer demand and lack of knowledge regarding inventory management, HS's inventory levels for raw material are $2.5M USD monthly when target is $1.85M USD, generating excess and obsolete inventory and losing the opportunity of working capital. In addition, the company does not currently have a standardized procurement pro-cess. For this project, 245 finished goods were classified, selecting 31 finished goods from a stratified sample. Finished goods were further broken down into 255 components to apply forecasts, Material Requirements Planning (MRP) and an Inventory Management System. After this analysis, logistics costs were re-duced by $ 1 M USD annually and forecasts were improved by 21%.

ABC Classification, Forecast, Inventory Management System, Liquidation Rate, MRP

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Introduction

HS is part of a multinational corporation that is one of the largest global manufac-turers of tools and storage (T&S), commercial electronic security, and engineered fastening systems with powerful growth platforms in the oil, gas, and infrastructure industries. HS Puebla is a wholly owned subsidiary of this corporation forming part of the T&S division in Mexico. HS is focused on satisfying customer demand and does not follow a standardized process or mathematical method to calculate accurate inventory policies (Mendoza, 2013). In contrast, when companies are capable of controlling their own inventory, they can reduce waste and increase working capital within the business (Rao, 2009).

According to Mendoza, some organizations base their demand and replenishment policies on qualitative approaches (Mendoza, 2013). Being a multinational compa-ny, HS should use qualitative approaches, however they do not follow an inventory system to procure the correct quantities of material for the production area. Nowa-days several methods for the planning and control of purchases exist to manage the correct material required for companies, such as re-order points, MRP, Kanban, or any other planning method supported by an ERP to control inventory (Jonsson, 2006). Small Business Administration or World Class companies should use invento-ry management systems and a standardized process to procure material; Supply Systems and inventory polices have been proven to improve management in the supply chain, optimizing the inventory supply to satisfy customer demand (Rojas, 2016).

This paper is focused on controlling inventory through an Inventory Management System and an improvement in forecasts.

Although there are several ways to resolve this problem, this paper analyzes current forecast reliability, improvement to the forecast, and inventory control through a systematic Inventory Management System that HS could use on a daily basis. Marin R. states the importance of the Supply Chain and using methods that help to achieve efficient production plans and satisfy customers; the right quantity of how much material to stock and a correct inventory classification are important ways to improve fill rates (Rusanescu, 2014). HS is cur-rently focused on Fill Rates, but they are not using the correct means to comply with internal and external customers. They are dealing with shortages, excess and obsolete inventory while using their current sourcing process. When HS standardizes their pro-curement process, they will receive benefits by reducing their total logistics costs as well.

Problem Description

There are certain key performance indicators (KPI´s) of upmost importance for the company such as Fill Rates (FR), inventory levels, inventory turnover, and work-ing capital. The company is facing nowadays a trade-off when trying to fulfill cus-tomer demand; HS is increasing inventory levels and not monitoring other KPIs. Cur-rent inventory levels and inventory turnover are 26% above target causing excess and obsolete inventory in the raw materials. Even though the inventory is meant to fulfill customer orders, there are unbalanced purchases that are not in accordance with the liquidation. Liquidation is an important KPI that refers to the transformation cost during production.

HS supplies their customers through Distribution Centers (DC). Each DC is respon-sible for supplying information to the corporate offices to forecast future require-ments; HS downloads this information through the JDA forecast system. The mate-rials department at HS is responsible for the Material Requirements Planning (MRP) for raw materials, and is the decision maker for the manufactured components of the finished goods or SKUs. During the first observation of the MRP, it was noted that HS does not classify their components by importance nor is there an inventory manage-ment system in place. Therefore, the process is overall general without applying any analytical methods.

Problem Root Cause

An Ishikawa analysis was performed to determine what might be causing these unbalanced inventory levels. In the following diagram, it can be observed that one of the causes of having an unbalanced inventory level is an incorrect sourcing process, especially in the MRP. This project will focus on the material requirements process, from the forecast calculation to the purchase order to fulfilling customer demand. Although quality and effective human resources are important, this project concen-trates on processes and methods.

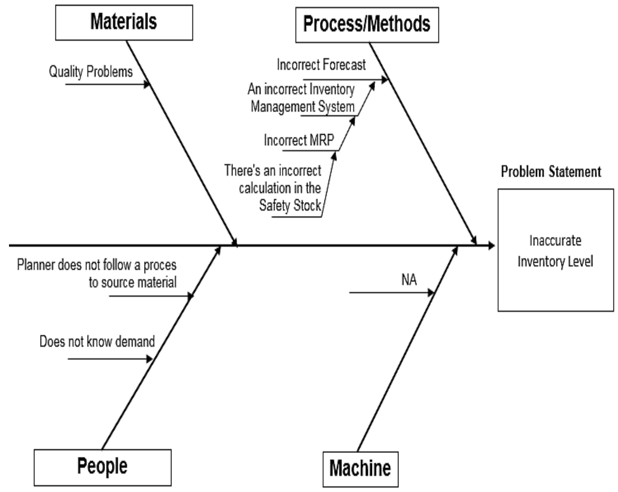

Figure 1 Ishikawa Inaccurate Inventory Level

Methodology

The initial study will begin by analyzing the fact pack of all the SKUs HS currently produces. The below methodology was analyzed within the company following a systematic, logical and mathematical method to plan and control activities. Steven C. proposes to maximize values and constraints of the current information and situation, starting from the beginning of the process and until the end; if there is a purpose in one direction, the rest of the process will embrace the changes (Cavaleri, 2012). The purchasing process was analyzed according to the current ISO 9001 certification. The following steps were taken to carry out the analysis.

Initiate an ABC analysis with all the finished goods considering two variables: liquidation and volume.

Verify the relation between these two variables with equation (1). These two variables are measured as KPIs by HS's corporate offices.

$$\varrho = \frac{\sum_{i=1}^{n}(X_i - \overline{X})(Y_i - \overline{Y})}{\sqrt{\sum_{i=1}^{n}(X_i - \overline{X})^2 \sum_{i=1}^{n}(Y_i - \overline{Y})^2}} \quad (1)$$

Utilize 80% of the SKUs resulting from the ABC analysis. The Pareto principle was used to generate a large output from a small input. Mohamed S. stated that Pareto is a powerful tool in the fields of purchasing and operational management within the Supply Chain (Ab Talib, 2015).

Validate the accuracy of the forecast, comparing the corporate forecast vs. the forecast calculated in this project.

Validate some SKUs using a stratified sample from the ABC analysis. Myoung L. proposes to use a stratified sample if strata does not depend on the response (Lee, 2011). This project focuses on validating the forecast regardless of the number of SKUs selected. Equations (2) (3).

$$n = \frac{N * z^2 * p * (1-p)}{z^2 p * (1-p) + e^2 (N-1)} \quad (2)$$

$$\binom{N}{n} = \frac{N!}{n!\,(N-n)!} \quad (3)$$

Analyze the demand of the SKUs: Coefficient of Variation for a time period of 12 months. Equation (4).

$$VC = \frac{\sigma}{|\overline{X}|} * 100 \quad (4)$$

Determine the dependent demand considering the scrap for each component.

Calculate the MRP considering current on-hand inventory and any open purchase orders (PO) with suppliers.

Obtain information for the Inventory Management: product, carrying, ordering and transportation costs.

In the Inventory management implementation, separate the items as direct purchase, consignment, and internal production; each type of item requires a different strategy for inventory management purposes.

Proposed systems are: Lot per Lot (L4L), average inventory, Economic Order Quantity (EOQ), and reordering point (ROP), equations (5) (6) (7) and (8) shown below.

L4L = Current_Period_Demand (5)

Average Inventory = Average_Demand_per period (6)

$$Q = \sqrt{\frac{2kd}{h}} \quad (7)$$

OP = Average_demand*Lead_Time (8)

Results

Correlation Variables

During the analysis process, there was an agreement with HS to use volume and liquidation as variables. Volume was selected as the first variable since it is important to determine which SKUs have a high rotation, and Liquidation was selected as the second variable since the efficiency of the company is measured based on this fac-tor. A correlation study was performed using equation (1) to review if these two vari-ables have dependency. The correlation obtained was high, 93%. It is accurate to use these two variables for the ABC analysis.

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ABC Analysis

Class	% Vol	% Liq	Total SKUs
AA	50%	65%	33
AB	14%	1%	5
AC	16%	0%	9
BA	6%	14%	16
BB	7%	10%	35
BC	2%	1%	14
CA	0%	1%	1
CB	1%	4%	16
CC	3%	3%	116
Grand Total	**100%**	**100%**	**245**

Table 1 Number of classes, ABC analysis, liquidation and volume

Having obtained nine classes, selecting 80% of the highest volume, a stratified sample was applied to each class to obtain the number of SKUs required for this pro-ject. After obtaining the number of SKUs, each SKU was selected by a random sam-ple so that each one had the same probability of being selected. The sample size stratified sample, formula (2). It is important to mention that all of the SKUs have the same probability of being selected since the goal is to select a representative quantity of SKUs to validate the current forecast. The significance level used to calculate the sample size in each group was 95%, where z = 1.96 and the probability of acceptance was p = 1%. This probability was used since all of the SKUs have the same importance and homogeneity; when the data is uncertain, p = 50% is typically used. Finally, the margin error used for this sample was 10%. The total number of combinations obtained for each class was determined from the formula (3).for each class was calculated with the

The following table shows the sample size and number of combinations per class.

Class	n	Combinations	Class	n	Combinations	Class	n	Combinations
AA	4	40,920	BA	4	1,820	CA	1	1
AB	3	10	BB	4	52,360	CB	4	1,820
AC	3	84	BC	4	1,001	CC	4	7,160,245

Table 2 Sample size and combinations per class

For the 31 SKUs, a random sample was also performed for each class; the total combination per class in the random sample was 7,258,261. Having selected the 31 SKUs for the analysis demand, the Coefficient of Variation (CV) was calculated for each SKU using formula (4). This formula was used to understand the data dispersion and variability. The coefficient of variation helps to understand the percentage variability of the standard deviation; if the percentage is high, data tend to be heterogeneous, while if the percentage is low, data tend to be homogeneous.

The results obtained for the CV were positive. From the 31 SKUs, only 3 had a CV superior to 30%; the other SKUs had a stable CV of less than 30%, meaning there is an ordinary fluctuation in the demand.

Forecast and Comparison Strategy

HS provided the historical sales data from 2014 until the end of 2015. This data was used to forecast the first semester of 2016. Richard H. states that the difficulty to forecast demand is found in the variability of market volatility, competitive pressures and product life cycle. It is important to use an accurate forecast method and an Enterprise Resource Planning system to run a successful Master Production Schedul-ing and hence, a correct MRP using the minimum working capital (Herrin, 2010).

As it is important to supply accurate forecast data using the different types of forecasting methods existing in the literature, R Studio® was selected as the forecast software to use for this project. R Studio® is a set of integrated tools designed with two forecast algorithms: exponential smoothing methods and a forecast algorithm with ARIMA applicable for seasonal and non-seasonal data (Hyndman, 2007). The work of Rob Hyndman allowed us to calculate an automatic forecast optimizing the parameters of the best model that fits the demand. At the end it was agreed with the company to add 10 more SKUs to use the majority of raw material in this project; the forecast results obtained with R Studio® were outstanding.

The summary in Table 3 details that the data forecasted with R Studio® was more accurate than the forecast used by HS. The methods used were various, but Multipli-cative and Additive without trend nor seasonal component were detected the most accurate. There was an improvement of approximately 21% in the Mean Average Deviation and in the Total Absolute Error. Both forecasts were on average below the real demand, however the forecast from R Studio® was closer to the actual demand than HS's forecast. Due to the forecast calculated with R Studio® providing im-proved results, this forecast was used with the 41 SKUs throughout the next steps of this project.

	R Studio	Current	R Studio	Current	R Studio	Current	R Studio	Current
	|Tot|	|Tot|	MAD (avg)	MAD (avg)	Err	Err	TS (avg)	TS (avg)
41 part # forecasted	448702	568145	1824	2310	-120832	-432047	-1	-5
Improvement	21%		21%		72%		76%	

Table 3 Forecast Improvement Summary

Below, the strategy to be followed to implement an inventory management system at HS is described.

- With the forecast calculated using R Studio®, perform a BOM explosion and execute a proper MRP to propose an inventory management system. Time period used, 6 months (January to June 2016)

- Calculate real operational costs during this 6 month period (January to June 2016), using actual HS purchases.

- Compare the total logistics costs incurred by HS vs the proposed methodology in this project.

- Estimate improvements in fill rates and operational costs.

BOM Explosion

The engineering team at HS supplied the complete BOM for all 41 SKUs. The BOM was exploded and the dependent demand was obtained. In this demand, HS was already considering the scrap for each raw material. After calculating the de-pendent demand, a total of 255 items that have to be acquired for the production of these 41 SKUs were obtained; Table 4 presents a summary below.

Tot Raw Mat	Description	Action
135	Direct Purchase	Implement an Inventory Management System
34	Internal Production	Will not be studied
86	Consignation	Recommend Safety Stock

Table 4 Dependent Demand

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The breakdown of the total 255 items is as follows: 135 items are direct purchases, so implementing an inventory management system to lower the total logistics costs is recommended. 34 items are produced internally and there is already a Kanban sys-tem in place to assure material availability, these parts will not be studied. The rest of the items are managed through consignment, and although the supplier is responsible for maintaining proper inventory levels, there is no policy or knowledge of what effi-cient inventory levels are.

Raw Material in Consignment

Every year, the buyer negotiates with most of the suppliers to start working under consignment; this is a good opportunity for the company to raise working capital when suppliers decide to work through this scheme. Only suppliers whose spend is higher than $30,000 USD are eligible for consignment.

The current consignment process at HS is to send a forecast to the supplier every 3 to 4 weeks, and the supplier will decide the inventory levels to be maintained at the HS facility. There is no policy with suppliers stating correct inventory levels, so the following process was suggested for the items handled under consignment:

- Take the real demand for the last 12 or 24 months for the items under con-signment.

- Maintain 4 weeks of inventory on average.

- Cycle inventory replenishment every 3.5 weeks.

- Calculate a safety stock with 98% confidence level considering a normal distribution.

Below the top five items in consignment at HS with the supplier's cycle replenish-ment and safety stock are extracted.

Part #	**U/M**	**SS**	**Cycle Inv**	**Tot Inv**
4643300	PZ	19,749	132,220	151,969
4643306	PZ	26,967	122,964	149,931
74207810	PZ	39,564	182,558	222,123
74207820	PZ	42,130	215,493	257,623
81800000	KG	59,799	314,898	374,697

Table 5 Safety stock and delivery quantity every 3.5 weeks

Raw Material Direct Purchase, Inventory Management System

For the remaining 135 items, the MRP was used to select the best inventory man-agement system for HS. To accomplish this task, the materials department provided: production and transit lead times for each item, current inventory in January 2016, Material cost, Ordering cost, Carrying cost and Transportation/Customs cost. Having collected the information above, the MRP was run for both cases, for the forecast calculated with R Studio® and for the real purchases from January to June 2016. Four different types of inventory acquisition were used: Lot per Lot (L4L), Economic Order Quantity (EOQ), average inventory, and Reorder Point (ROP). These systems were used as it has been proven that frequent order releases lower inventory and re-duce the need for continuous forecast adjustments (D'Avino, 2013), plus the compa-ny is aligned to not place large orders as the space in the warehouse is limited. The best result was the reordering point, which should be considered the new method for the MRP with suppliers.

Benefits

The benefits obtained in this project were exceptional.

First, the forecast was im-proved by 21%, which does not only imply that purchases will be more accurate, but closer to the real demand. When analyzing the tracking signal in the forecast calcu-lated by R Studio®, on average it is closer to the real demand, while HS's forecast is inaccurate. Using this data would ultimately increase customer FR. Table 6 shows that both forecasts were calculated below real demand, but the forecasts from R Studio® were significantly better.

	Tot Items	% Err
Real Demand	1,495,533	-
HS Forecast	-432,047	-29%
R Studio Forecast	-120,832	-8%

Table 6 Forecast total error below real demand

On the other hand, the total logistics costs obtained with each of the inventory management systems in the 6 month period was $244,507USD. The opportunity to improve the current sourcing process at HS is feasible, and it is important to restructure their current procedure as soon as possible.

L4L Cost	EOQ Cost	Avg Inv Cost	ROP Cost	HS Cost
1,542,731	2,845,588	1,451,308	1,273,594	1,518,101

Table 7 Logistics Costs Inventory Management vs Current HS Operation

Conclusions and Limitations

Multinational companies usually have people responsible for forecasting customer requirements and smoothing the information according to customer needs. HS never validated its forecasts in the past and do not have a standardized process to procure material to satisfy customer requirements. This project detected some weaknesses in the material requirements planning process and it was able to improve the forecast and standardize the procurement process by implementing an inventory manage-ment system. Logistics costs were reduced by $0.5M USD and forecast reliability was improved by 21% focusing on SKUs extracted from a stratified sample. However, it is important to implement a standardized procurement process for all of the raw ma-terials currently used in HS. Although this project was successful in its approach, there are two points to review further: (1) the forecast needs to be readjusted for all of the corporate manufacturing plants before doing any changes to HS, and (2) a further analysis of the inventory suggested for consignment, and the order suggestions are not a limitation regarding the space in the warehouse, some suppliers under consign-ment might have to deliver more frequently due to the volume of their products.

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Anthropometric indicators that best estimate adiposity: a systematic review

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Abstract

To estimate adiposity, a good anthropometric indicator should be objective, valid, reliable, capable in detecting health risk and offer results of interventions by the change in body composition. Given the variety of possible indicators, it is important to establish which are the most used and validated; so the objective of this systematic review was to identify the anthropometric indicators that best estimate adiposity in young adults. A systematized search was made in PubMed, ScienceDirect, Scopus and Cochrane Library, with the descriptors anthropometry, anthropometric indicators, adiposity, obesity, validity, dual x-ray, adult and plethysmography. Methodological quality of the articles was evaluated and those who appraised the validity of anthropometric indicators against an image gold standard, were taken into account. The relationship between body mass index, waist circumference and body adiposity index was studied in the 4 included articles, determining that the first two are considered the best anthropometric indicators to estimate adiposity

Anthropometric indicators, validation, adiposity, adults

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Introduction

Anthropometric indexes usually refer to proportions of body measurements, which are given an interpretation, hence that body weight acquires a better meaning when it relates to age or size of the individual, than when expressed alone. Some indicators are useful for assessing body composition as part of an individual's physical performance or nutritional status or in the detection of health risks (WHO, 1995).
Body mass index (BMI) is one of the most widely used anthropometric indicators for its low cost and simplicity of calculation of excess weight and its use at an international level was accepted by the WHO in adult individuals since 1995 (Rosales, 2012)

Strong criticism of the BMI for its variation in age, gender, and ethnicity, and failure to distinguish between fat and lean mass despite their relationship with cardiometabolic diseases (Eknoyan, 2008; Nutt, 2015; Garrow & Webster, 1985) allowed the emergence of other indexes such as waist / hip (WHR), or waist / height (WHtR) that despite its correspondence with fat accumulation in the abdominal area, have not been characterized by effectively identifying some risk factor for health (Huxle, Mendis, Zheleznyakov, Reddy & Chan, 2010). On the other hand, waist circumference (WC) is recognized as an indicator of central adiposity and proven as a metabolic risk factor, although it also neglects other regions of accumulation of adipose tissue and does not quantify total body fat (Lean, Han & Morrison, 1995; Pérez, Gálvez & Miranda Pérez, 2009).

The anthropometric variables have been used in prediction equations for the estimation of fat percentage, with the inconvenience of errors related to the compressibility of skin and subcutaneous tissue, as well as to estimate a fixed relationship between internal and external adiposity, among other things (Pretice & Jebb, 2001).

Recently the body adiposity index (BAI) has been satisfactorily validated against modern imaging methods, although it does not properly determine the fatty tissue content since its formula includes only the perimeter of hip in relation to height (Pan American Health Organization, 2000). On the contrary, more sophisticated equipment such as computerized axial tomography (CAT), magnetic resonance imaging (MRI) or dual X-ray absorptiometry (DEXA), which estimate adipose tissue with great precision, have served as gold standards for the validation of anthropometric indicators, but their use is limited in large-scale studies because of their high costs (Demmer, et al., 2016; Hames, Anthony, Thornton & Goodpaster, 2014).

A good anthropometric indicator should adequately reflect the problem, which in this case is the content of body adiposity; and in view of the variety of parameters, it is important to establish which of those used in clinical practice meet their objective, which are reliable to detect the risks and which facilitate the integral diagnosis of adiposity to be used in the prevention of related pathologies. Therefore, the objective of this systematic review was to identify the anthropometric indicators that best estimate adiposity in young adults.

Metodology

Search strategy

The electronic databases consulted were PubMed, ScienceDirect, Scopus and Cochrane Library. We searched for articles related to the identification of validated anthropometric indicators that best estimate adiposity in young adults with the descriptors anthropometry, anthropometric indicators, adiposity, obesity, validity, dual x-ray, adult and plethysmography, in English and Spanish, related to the identification of validated anthropometric indicators that best estimate adiposity in young adults delimited from January 2010 to December 2016.

Studies selection

Included were original studies evaluating the validity, correlation and/or concordance of anthropometric indicators against a gold standard of imaging in young adult males and females. Those studies done in children or with some associated pathology were excluded.

A total of 727 articles with established descriptors were identified. After reading and analyzing the abstracts, 699 articles were excluded because they did not meet the inclusion criteria. Of the remaining 28 documents, 24 were discarded because they were repeated in the databases; so that after full reading, four articles were included for this study (n = 4). Figure 1 shows the process of selecting articles.

Search strategy

In the electronic databases PubMed, ScienceDirect, Scopus and Cochrane Library we searched for articles with the descriptors anthropometry, anthropometric indicators, adiposity, obesity, validity, dual x-ray, adult and plethysmography, related to the identification of anthropometric indicators validated that best estimate adiposity in young adults, in English and Spanish, limited to the period from January 2010 to December 2016.

Studies selection

Included were original studies evaluating the validity and/or correlation and/or concordance of anthropometric indicators against a gold standard of imaging in young adult males and females. We exclude those studies done in children, adolescents and older adults, or with some aggregate pathology.

A total of 727 articles were obtained with the descriptors established, identified by the titles of interest. After the reading and analysis of the abstracts, 699 articles were excluded because they did not meet the inclusion criteria, since the analyzes were done in children or older adults, or with some type of aggregate disease. Of the remaining 28 documents, 24 were discarded because they were repeated in the databases; so only after full reading, only four articles were included for this study (n = 4). Regarding the use of a gold standard for validation, only the use of DEXA in young adults was identified. (See Figure 1).

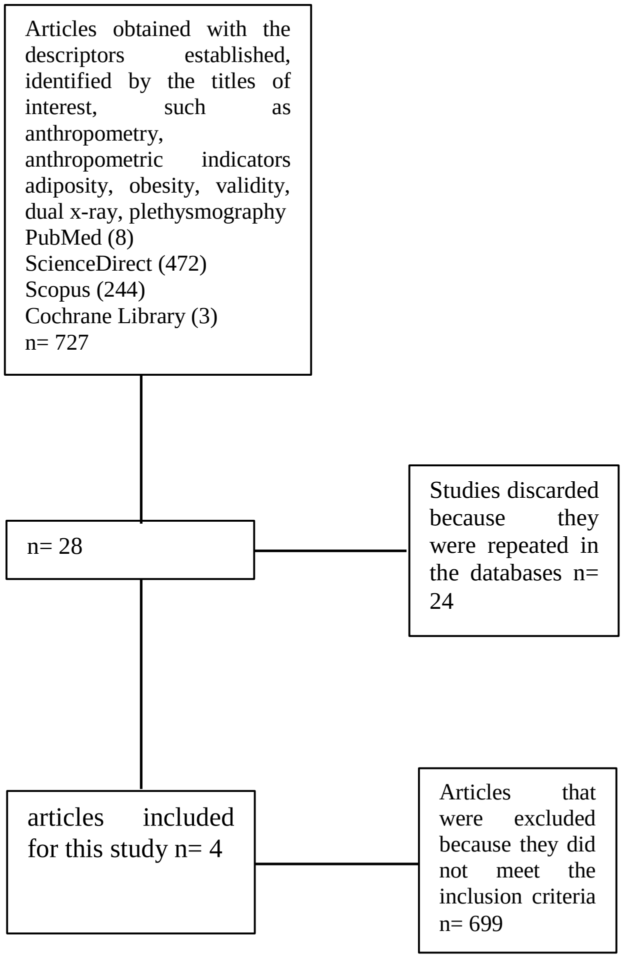

Figure 1 Studies selection process

Quality assessment

The quality of included studies was determined by the List of Downs and Black, an instrument comprising 27 items divided into 5 measurement subscales. According to the type of studies used here, 11 items were taken regarding the timely reporting of the methodological process, the validity of the sample and the results presented. The studies with the 11 positive items were considered of good methodological quality.

Results

The anthropometric indicators that have been most validated to estimate adiposity in young adults (Table 1) are BMI, WHR and BAI. DEXA was identified as the reference method. In all studies Pearson's correlation was used for statistical analysis; in terms of methodological validity the total of articles were of good quality with 11 positive items for each according to the List of Downs & Black.

Sun, Vam Dam, Spiegelman, Heymsfield, Willett & Hu, 2010, reported the validation of BMI and WHR, as well as the correlation of these with triglycerides, cholesterol, glucose, insulin and C-reactive protein. The sample analyzed in this review corresponded to n = 3,960 of which were males with n = 2,049 and females n = 1,911, were also adults classified by gender, race and age, statistical analysis for the present systematic review were taken from the data corresponding to men and women between 20 and 39 years of age, presenting in women a r = 0.92 and in men r = 0.95 compared to the comparison of BMI and percentage of fat by DEXA. Regarding the correlation of WHR with DEXA, the values were r = 0.95 in men and r = 0.93 in women. It was concluded that both BMI and WHR are valid adiposity indicators against the measurements obtained by the DEXA.

In order to find also the relationship between BMI, WHR and adiposity data offered by DEXA, (Kim, et al., 2014) with data from the Fourth and Fifth National Health and Nutrition Survey of Korea, 18,198 subjects were analyzed between men and women of different age groups, of which, for the purposes of the present review, data were collected from 5,843 men and women from 19 to 39 years old.

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A positive correlation was obtained between the percentage of fat obtained by DEXA and WHR with r = 0.72 for men and r = 0.63 for women. While, with BMI in men it was r = 0.71 and in women r = 0.70, concluding that both BMI and WHR reflect body fat.

In 2011, Bergman et al., with the purpose of counteracting some of the limitations of BMI proposed BAI; the formula is BAI = [(HC, in cm)/((h, in m)1.5)$^{-18}$)] where:

WC = hip circumference in centimeters

h = height in meters

The equation was tested on 1,733 Mexican-American subjects. The results of this study showed a positive correlation between BAI and the percentage of body fat estimated by DEXA with r = 0.85, concluding that this indicator estimates adiposity directly.

Yu et al., in 2015 in order to test whether BAI is a better indicator than BMI and WC in Chinese adults, these three indicators were contrasted against DEXA. The age of the sample evaluated was 18 to 65 years old, corresponding to n = 5,726, of which 872 were men and 4,854 women. The results of the correlation between BMI and DEXA were, in men with r = 0.66 and r = 0.77 in women; a correlation between WC and DEXA found r = 0.71 and r = 0.70 in men and women respectively; for BAI r = 0.44 in males and r = 0.64 in females. The authors concluded that the BMI and WC are better indicators of adiposity in Chinese population than the BAI.

Autohr(s)	Sample	Indicador validado	Results	Observations
Sun et al., (2010)	n=31,136	BMI WC	BMI M (r= 0.92) F (r= 0.95) CC M (r= 0.95) F (r= 0.93)	For this review only young adult data were analyzed
Bergman Et al., (2011)	n=1,733	BAI	r = 0.85	The results are from the sample total.
Kim et al (2014)	n=18,198	BMI WC	BMI M (r= 0.64) F (r= 0.68) CC M (r= 0.67) F (r= 0.63)	For this review only data from young adults was analyzed
Yu et al. (2015)	n=5726 adults n=2425 children	BMI WC BAI	BMI M (r=0.66) F (r= 0.77) CC M (r =0.71) F (r = 0.70) BAI M (r = 0.44) F (r= 0.64)	For this review, only data from adults was analyzed
BMI=body mass index, WC=Waist Circunference, BAI=body adiposity index, DEXA=dual X-ray absorptiometry, M=Male, F=Female, *r*=Pearson Correlation				

Table 1 Articles analyzed in this review

Discussion

Because the location and body distribution of fat is important because of its contribution to disease development (Vague, 1947, 1957), it has been necessary to explore the validity of other anthropometric indicators used to estimate adiposity, such as WHR, WC and BAI .

The WHR has lost utility because in many individuals the same ratio between the two circumferences is maintained despite the increase in weight. On the other hand, in spite of the different sites of measurement of WHR, this parameter retains high correlation with central obesity.

Selecting the best indicator involves taking the results it provides, such as criteria that refer to objectivity, validity and reliability; to the cut-off points established for it; the data for the prediction of risk factors and the result of the interventions applied to a subject (WHO, 1995). The article by John J. Himes in 1995, which was part of a document issued by the Pan American Health Organization, describes as anthropometric indicators for obesity and distribution of body fat to BMI, relative weight, sum of skinfolds, the circumferences of the body, the relationships between them and the prediction equations of total body fat. But at the time of matching these indicators, the result was poor to identify populations with higher adiposity.

According to the above, it is likely that the only anthropometric indicators that comply with these principles are BMI and WC, so in the present review, only those were identified with those criteria.

The BAI recently proposed, its own name and methodology of validity, coincided with the search features proposed here, so it was also taken into account, however it is still necessary to clearly define their respective cutoff points.

One of the advantages offered by DEXA is the determination of total body fat and segmented by anatomical regions, the results are obtained in kilograms (absolute weight) and percentage of fat (%F). The study by Sun et al. Determined that both BMI and WC have validity against DEXA despite differences between the ages, sex and race of the sample studied. The DEXA is not able to distinguish visceral or subcutaneous fat so that in that study did not establish a correlation at this level. In Kim et al., in the Korean population, the total adiposity measured by DEXA was obtained in absolute weight (kg) and %F and segmented in body regions: head, arms, legs and trunk. Both BMI and WC had a good correlation with DEXA and even more in women, but at an older age, this ratio decreased. It should be taken into account that this sample was only in a single population type and ethnic characteristics marked differences in the distribution and accumulation of body fat, even the study did not present the data of abdominal adiposity by DEXA, which is fat which more cardiovascular risk represents.

For its part, the BAI with a high validity against DEXA in Mexican and African American population, makes it specific for this type of population, leaving aside the white race. This latter fact was ratified by Yu et al., when evaluated in Chinese population, finding that it correlates in a lower proportion against DEXA.

Although new studies have validated the BAI and the results indicate that it can be a good indicator, differences are observed in terms of age, gender, in people with some type of aggregate pathology or in sports practices, so their use may be limited.

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Conclusion

Although the BMI is not able to distinguish between fat mass and lean mass, and WC is used for the estimation of abdominal adiposity, these two have proven to be the best anthropometric indicators to estimate adiposity due to its high correlation with direct methods like the DEXA. Since the location and body distribution of fat predisposes to the development of chronic non-transmissible diseases of high global prevalence, it is important to identify their distribution, which makes it necessary to explore the validity of other anthropometric indicators that can be used to estimate adiposity.

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Phenol biodegradation at high organic loads in a complete sludge reactor by activated sludge

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Abstract

The presence of phenols in industrial discharges have phenol concentrations between 35 and 400 mg/L. But there are extreme cases, with concentrations of 30 to 80 g/L. The methods used for its treatment include: degradation, elimination and recovery. Its biological treatment is complicated because it causes the inhibition of microorganisms. The objective of this work was to evaluate the effect of the organic load on the phenol biodegradation rate of an industrial effluent. An activated sludge reactor was used at 1.76 and 2.81 days of hydraulic retention time (HRT), 25±0.5°C and air flow of 2.5 L/min, without pH control. The results showed a HRT of 1.76 days, with an organic load of 11.2±0.3 kg COD/$m^{3}\cdot$d (run I), a lower COD removal rate, compared with the phenol biodegradation rate (30 and 41%). At 7.97±0.12 kg COD/$m^{3}\cdot$d (experiment II) and the same HRT, the COD removal rate was higher compared to phenol biodegradation (56 and 37%). And with 3.3±0.2 Kg COD/$m^{3}\cdot$d) (experiment III), the rate of removal of COD as of phenol biodegradation was 34% at 2.81 days of HRT.

Phenols, Toxicity, Biodegradation of Phenol, Activated Sludge, Catechol

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Introduction

Phenol and its by-products are some of the most widely studied organic pollutants due to their toxicity to living things and the environment. Phenol and its byproducts are some of the most extensively studied organic pollutants due to their toxicity to living beings and the environment (Agencia de Protección al Ambiente de EEUU, ATSDR, 2016).

Phenolic pollutants discharged from different kind of industries, such as pesticides, paints, polymer resins, paper, and petrochemistry have been found in their effluents (Ahmaruzzaman, 2008; Lin et al., 2009). As well as those discharged by the oil processing industry and refineries, which contain various compounds; Fats and oils, sulfates, suspended solids, cyanides, nitrogen compounds and heavy metals such as chromium; Iron, nickel, copper, molybdenum, selenium, vanadium and zinc. Organic compounds, such as: aliphatic and aromatic hydrocarbons, sulfur compounds, nitrogen compounds and phenols in concentrations higher than 30,000 mg/L (Wake, 2005). Effluents from coke ovens and pharmaceuticals have phenol concentrations between 10 and 300 mg/L (Lepik and Tenno, 2011; Pramparo et al, 2012). However, the presence of phenol in wastewater has been reported with concentrations up to 10,000 mg/L (Krastanov et al, 2013).

According to section 313 of Title III Emergency Planning decreed by the EPA (2015), phenol by having in its structure a benzene ring, i considered a pollutant priority due to its high toxicity and low biodegradability, in addition to being considered carcinogenic, mutagenic and teratogenic. it is easily absorbed by the skin and mucous membranes of animals and humans.

Its toxicity directly affects a great variety of organs and tissues, mainly lungs, liver, kidneys and genitourinary system (Olujimi et al., 2010).

Finding in upper freshwater and marine organisms, minimum values of CL (lethal concentration) or EC (critical exposure) in crustaceans and fish between 3 and 7 mg/L phenol (ATSDR, 2016).

In the literature, treatment technologies for phenolic compounds are addressed: the first consists of chemical processes oxygenation with reagents such as hydrogen peroxide (Qayyum et al., 2009) and the second of the adsorption and extraction processes (Lin and Juang, 2009; Smith et al., 2009). Other technologies contemplated chemical coagulation (Ozbolge et al., 2002), solvent extraction (Yang et al., 2006), membrane techniques (Kujawski et al., 2004), microfiltration (Wei et al., 2004), inverse osmosis (Ipek et al., 2004), biodegradation (El–Naas y Makhlouf, 2008), chemical oxidation (Suarez-Ojeda et al., 2007) and electrochemistry (Yavuz et al., 2006).

The conventional processes in the detoxification of this type of compounds have proved to be efficient, but they present certain disadvantages and limitations, due to the fact that, at concentrations of 10 mg/L phenol, causes inhibition of microorganisms. Their treatment through these processes requires extreme operating conditions, leading to the formation of intermediates, which, far from solving the problem, contribute to water pollution. Under this scenario, its toxic effect has been extensively studied using microorganisms (bacteria, fungi, protozoa, and algae) and numerous vertebrates and aquatic invertebrates.

Therefore, prokaryotic and eukaryotic organisms under aerobic respiration conditions can carry out its degradation with oxygen being the final acceptor of electrons, using carbon molecules to produce CO_2, H_2O and energy in the form of ATP (Rodríguez, 2003).

With the use of microorganisms, decontamination is achieved by effectively eliminating these compounds, since bacteria, protozoa, and other major microorganisms disintegrate most organic compounds such as phenol, by reactions that use oxygen, transforming it in substances rich in energy and in substances of lower energy. The treatment of industrial effluents with high concentrations of phenol by activated sludge is an alternative for the control, correction and regeneration of the ecosystems affected by discharges of this nature.

The aerobic pathway has shown that there is a common metabolic pathway for this type of compound and even for those not so close to the phenolic compound family as biphenyls (Autenrieth et al, 1991). During which, the oxygen is consumed, and by the action of the enzyme phenol monooxygenase, an $^{-}$OH group is added to the phenolic ring resulting in the formation of catechol. In this way, the catechol ring can be broken in two different ways, by the *ortho* route and by the meta route. During the *ortho* route, the catechol bond 1-2 is ruptured to produce the muconic acid (Figure 1).

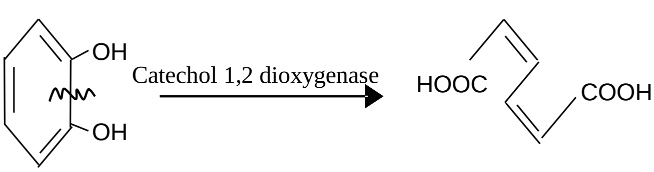

Figure 1 Ortho rupture of the phenolic ring

By the meta route, the ring rupture occurs between carbons 2-3, to give rise to the formation of the 2-hydroximuconic semialdehyde (figure 2).

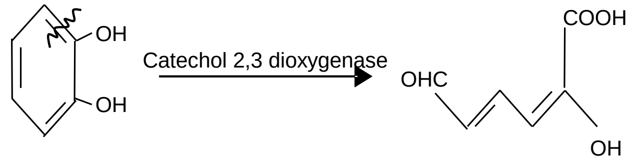

Figure 2 Meta rupture of the phenolic ring

In this route, after the rupture of catechol catalyzed by the enzyme catechol 2,3-dioxigenase, the 2-hmas can be degraded in two different ways as shown in Figure 3. In the first, the 2-hmas is oxidized to give rise to the formation of 2- hydroximuconic acid, which is subsequently decarboxylated through the action of two enzymes, an isomerase and a decarboxylase, to form 2-oxopenta-4-enoic acid. For its part, the 2-hmas is fractionated by hydrolysis to produce the acids; formic and 2-oxopenta-4-enoic acid. The latter degraded by hydration under the action of an aldolase to 4-hydroxy-2-oxopentanoic acid and then to acetaldehyde and pyruvic acid respectively, which continue to oxidize upon incorporation into the Krebs cycle (Ramírez, 2005).

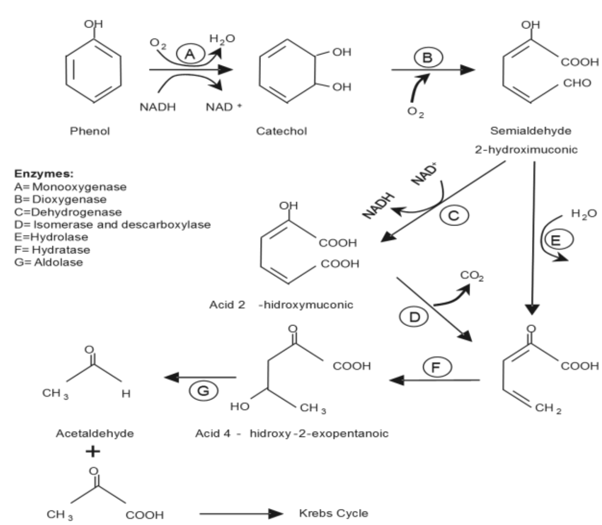

Figure 3 Meta pathway of aerobic phenol biodegradation (Shalaby, 2003)

Genes that encode the pathway enzymes *meta* in the bacteria, are part of large plasmids such as TOL, while those encoding the pathway enzymes *orto*, most are located in the DNA (Selesi et al., 2010).

The success of phenol biodegradation in wastewater, It depends on the strategy employed during the acclimation of the bacterial consortium (biomass) of the biological reactor to the presence of this type of toxic compounds, what results a key factor in achieving the highest rate of biodegradation (Terreros et al., 2016). Since its bactericidal effect of phenol, Is based on the ability of the compound to dissociate within the cells, provoking that the functions of the cytoplasmic membrane are disrupted, causing cell death (Tay et al., 2005).

Biodegradation by biological processes, involves many factors. Among them; temperature, pH, because each microorganism has a specific range of temperature and pH for his growth (pH=7.0) (El-Naas et al., 2009).

Whilst extreme values of pH (less than 3 or greater than 9) are inhibitory for growth (Agarry et al., 2008). Other important factors are; dissolved oxygen concentration, concentration of substrate (Trigo et al., 2009) and the organic loading rate (Liu et al, 2003a). That is to say, a relatively high organic load facilitates the formation of anaerobic granules in a system UASB. In contrast, there are evidence to suggest that aerobic granules can be formed over a wide range of organic charge rates, ranging from 2.5 to 15 Kg COD/m^{3}·d. With an increase in the organic load of 3 to 9 Kg COD/m^{3}·d, the size of the aerobic granules increases 1.6 to 1.9 mm (Liu et al., 2003a).

Therefore, an increase in the organic loading rate can raise the rate of growth of the biomass, but in turn, can reduce the strength of the structure of the microbial community.

However, the physical characteristics of the aerobic granules, depend on this velocity. Which may affect their morphology, density, specific gravity and volumetric index of the sludge (VIS). The physical strength of aerobic granules may decrease with increasing speed of organic loading. At high loading speeds, it can occur partial loss of the integrity and consequently, the disintegration of its granular structure (Liu et al., 2003b).

Among the bacterial strains that degrade phenol may be mentioned: *Acinetobacter calcoaceticus, Pseudomonas pickettii*l, *Klebsiella oxytoca*, *Ralstonia eutropha*, *Burkholderia cepacia* G4, *Pseudomonas putida* (Kwon and Yeom, 2009), *Rhodococcus opacus* (Matera et al., 2010), *Alcaligenes* cepa TW1 (Essam et al., 2010). Levaduras como: *Candida tropicalis*, *Rhodotorula rubra* y *Trichosporon cutaneum* (Komarkova et al., 2003).

Algae (*Ochromonas dánica*) and fungus (Actinomicetes, *Nocardia hydrocarbonoxydans*) with activity to biodegrade phenol (Busca et al., 2008).

The application of microbial consortia in biological processes, presents some advantages over pure cultures. Between them, the increase in the degradation rate of phenol, by allowing the bacterial consortium exceed any event that limits the complete biodegradation of phenol (Cordova et al., 2009).

For its part, the presence of more than one organic compound in the system can affect the functions of biodegradation. Many studies have reported inhibitory effects or increase in phenol degradation systems by adding glucose or phenolic compounds. When placing a co-substrate, it can improve, reduced or not affect the biodegradation of contaminants such as phenol (Bajaj et al., 2008). For example, Arutchelvan et al (2006), observed that by adding dextrose as co-substrate in ranges of 0.2 to the 0.8% (p/v), decreased phenol degradation efficiency. Since dextrose because it is a carbon source of easy biodegradation, the microorganism ignores phenol as a source of carbon, and in consequence, the period of its degradation, was delayed.

Acclimatization of any type of microorganism to the presence of phenol for its biodegradation, is a key factor (Terreros et al., 2016). Yoong (2000) mentions that at concentrations greater than 1300 mg/L of phenol during the treatment of wastewater by activated sludge, provoke complete inhibition of the system.

Silva et al (2002) used an SBR reactor, achieving a phenol biodegradation of the order of 99%.

Bevilaqua (2002) studied a conventional aerobic system coupled to an enzymatic treatment using tyrosinase as an enzyme, and observed degradation performance of the 75% with a residue of 420 mg/L of phenol in a reaction time of 4 hours with 46 Um/L of tyrosine and 50 mg/L of chitosan as coagulant).

Jiang et al (2004) investigated the possibility of treating phenolic wastewater with aerobic granular sludge, which showed an excellent capacity to degrade it to a concentration of 500 mg/L.

Tay et al (2005) used four reactors inoculated with aerobic granules, with feed sequenced with acetate as the main source of carbon, with a mass loading of 3.8 $Kg/m^{3\cdot}d$. Subsequently, the reactors were fed with different loads phenol (0.6, 1.2 and 2.4 $Kg/m^{3\cdot}d$). The reactor whith a load of 0.6 $kg/m^{3\cdot}d$, completely degraded the phenol at 60 min, while the reactor with the charge of 1.2 $Kg/m^{3\cdot}d$, it completely removed in 90 min. But, with 2.4 $Kg/m^{3\cdot}d$ present problems removing it.

Melo et al (2005) studied the biodegradation of phenol in a system of biological reactors; one discontinuous and one rotating, fed at 2 different flow rates: 2 y 4 L/h. Confirming that the performance of the system, improved to increased availability of dissolved oxygen and stirring speed, which favored the transfer coefficient of the oxygen mass, achieving a better degradation of phenol.

Hossein et al. (2006) used a packaged bubble bioreactor for the treatment of phenolic residues, finding 100% of its elimination at a loading rate of 33120 $mg/m^{2\cdot}hr$.

Marrot et al. (2006) studied the biodegradation of high phenol concentration by activated sludge in a membrane bioreactor with phenol concentrations of 0.5 to 3 g/L. Reporting that the activated sludge process cannot stand the phenol at an excessive loading speed.

Bajaj et al. (2008) in a reactor with a cycle of 360 minutes of operation (260 minutes under aerobic conditions and 100 minutes under anoxic conditions). They found a 50% removal of phenol present in synthetic wastewater with an initial concentration of 5.17 g/L of phenol.

Contreras et al. (2008) used respirometric techniques to study the effect of pH, phenol and dissolved oxygen concentrations during the kinetics of phenol degradation by activated sludge, with a purity of 99%, a hydraulic retention time (HRT) of 24 h and air flow of 2 L/min and dissolved oxygen concentration (DO) above 5 mg/L. Observing that both the pH and the concentration of dissolved oxygen have a significant effect on phenol degradation.

Farooqi et al (2008), studies on biodegradation of phenols and m-cresols by upflow anaerobic sludge blanket and aerobic sequential batch reactor. The results indicates that anaerobic treatment by UASB and aerobic treatment by SBR can be successfully used for phenol/cresol mixture, representative of major substrates in chemical and petrochemical wastewater and the results shows proper acclimatization period is essential for the degradation of m - cresol and phenol. Moreover, SBR was found as a better alternative than UASB reactor as it is more efficient and higher concentration of m cresols can be successfully degraded.

Donoso-Bravo et al. (2009) using synthetic phenol water with a concentration of 5 gCOD/L and a content of; 10, 25 and 40% phenol as carbon source at a concentration of 400 mg/L in ASBR reactors. They found a biodegradation efficiency of the order of 30%.
Chérif et al (2011) studied a model to explain the specific growth rate of microorganisms associated with substrate consumption and the effect of an inhibitor on the degradation of phenol with a purity of 99% in a batch reactor of 2 L of working volume at 25±1°C with a phenol concentration range of 0-793 mg/L, biomass concentration of 0.74 to 6.7 g/L and air flow of 2.5 L/min.

Finding that the model-based design of fed-batch feeding strategies allowed the phenol degradation to be conducted separately under the modes of substrate limitation and substrate inhibition.

Fernandez et al (2013), studied the aerobic biodegradation of a mixture of mono substituted phenols in a sequencing batch reactor. The PNP and o-cresol mixture was also biodegraded although some transitory accumulation of intermediates occurred (mainly hydroquinone and catechol) o chlorophenol was not biodegraded and resulted in inhibition of o-cresol and PNP biodegradation and complete failure of the SBR within a few days. The biomass had very good settling properties when a settling time of 1 min was applied: sludge volume index (SVI_5) below 50 mL/g, SVI_5/SVI_{30} ratio of 1 and average particle size of 200μm.

Athar et al (2015) studied in an SBR reactor, the treatment of synthetic residual water with phenol. Reporting that by increasing the phenol concentration at 2000 mg/L during the acclimatization phase, affects the activity of biomass due to its toxicity.

Inglezakis et al (2016), Studied the inhibitory effect of cyanide, phenol and 4-nitrophenol in a activated sludge reactor, evaluating the degree of inhibition on aerobic oxidation of organic matter, nitrification and desnitrification. Using cyanide, phenol and 4-nitrophenol of 0.2 to 1.7 mg/L, 4.8 to 73.1 mg/L, and of 8.2 to 73.0 mg/L respectively. And they report that was highly toxic cyanide, inhibiting the autotrophic activity of biomass by more than 50%, as well the heterotrophic activity and of the desnitrification, to low concentrations (1.0 a 1.7 $mgCN^-/L$).

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Mentioned that bacteria autotrophic were more sensitive to phenol that the aerobic heterotrophs, while denitrifying bacteria, were more resistant to phenol. In this context, the use of mixed microbial cultures, principally by activated sludge, is an excellent alternative for phenol biodegradation (Badia-Fabegrat et al., 2014; Pradeep, 2015).

The objective of this work was to evaluate the effect of the organic load on the rate of removal of COD and phenol from an industrial effluent by activated sludge, varying the hydraulic retention time, in order to achieve maximum removal.

Materials and methods

Sampling

There were 3 batches of 10 L of phenolic wastewater. The method used for sampling is described in the standard (NMX-AA-003-1980).

Analytical techniques

For the evaluation of the main parameters in the industrial effluent phenol feed (influent) of processed water (effluent) and control system studied, the following analytical techniques were used:

The pH was evaluated by a potentiometer (Conductronic PC18). COD, total solids (TS), volatile solids (VS) were determined according to standard method (APHA, 2016). The determination of phenol, was performed by the colorimetric method of the 4-aminoantipyrine according to the Mexican standard NMX-AA-050-SCFI-2001 using a UV-VIS Spectrometer Perkin Elmer Lambda XLS model computer.

Experimental design

A complete mixing aerobic reactor was used, with a design volume of 4.28 L, useful volume of 3.87L, with dimensions: Length: 28 cm, width of 17.5 cm and depth of 13 cm, divided into 4 sections (A, B , C and D). Section "A", where the biological reaction is carried with dimensions: Length of 18.3 cm, width of 17.5 cm and depth of 13 cm. Section "B" (sludge return zone) to section "A", with a length of 10.2 cm, width of 6.6 cm and depth of 12.4 cm. Section "C" (sedimentation zone) with a length of 7 cm, width of 6.6 cm and depth of 12.3 cm and section "D" (zone of clarification) with a length of 17.5 cm, width of 2.5 cm and depth of 10.4 cm (figure 1), to have a hydraulic behavior in cascade. The system used was equipped with a thermostat to maintain the temperature at 25±0.5°C, fine bubble diffusers and air pump.

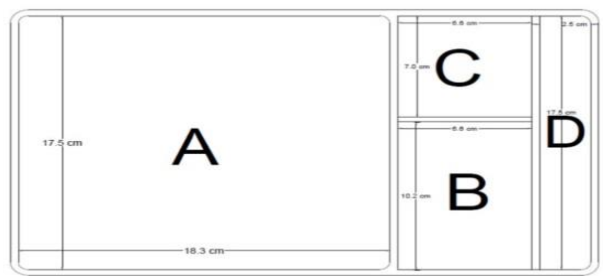

Figure 4 Schematic of the activated sludge reactor

Inoculum

The biomass used as an inoculum was collected from an activated sludge reactor at the Cerro de la Estrella municipal wastewater treatment plant in Mexico City, with a concentration of 12.6 g/L of TS and 9.6 g/L of VS.

Alimentation (influent)

Before analyzing the results, Table 1 shows the averages of the main parameters evaluated in 3 lots of 10 L of phenolic residual water, through calibration curves. A significant dispersion is observed in the data, due to the variability of phenolic wastewater during the different sampling periods.

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Parameter	Experiment		
	I X±S	II X±S	III X±S
COD (g/L)	19.73±3.36	14.04±1.9	9.27±1.7
Phenol (g/L)	2.81±0.35	3.21±0.7	3.18±0.3
pH	6.56±0.19	6.65±0.14	6.66±0.12
TS	0.32±0.2	0.25±0.1	0.26±0.1
VS	0.19±0.1	0.19±0.08	0.17±0.1
X: arithmetic average, S: standard deviation			

Table 1 General characteristics of industrial residual water with phenol (influent)

Operating conditions of the reactor

The table 2 shows the operating conditions of the reactor with continuous feed flow, to the different runs in which the experiment was carried out.

Experiment	I X±S	II X±S	III X±S
Bv (kgCOD/m$^{3}\cdot$d)	11.2±0.3	7.97±0.12	3.3±0.18
HRT (days)	1.76	1.76	2.81
Q_{air} (L/min)	2.5	2.5	2.5
X: arithmetic average, S: standard deviation			

Table 2 Operating conditions of the activated sludge reactor

Results and discussion

Characteristics of phenolic wastewater after treatment. The table 3 shows the averages of the main parameters evaluated for the water treated by the activated sludge reactor, during the experiment under the tested operating conditions.

Parameter	Experiment		
	I X±S	II X±S	III X±S
COD (g/L)	13.65±3.16	6.24±1.6	6.08±0.9
Phenol (g/L)	1.67±0.4	2.01±0.37	2.1±0.27
pH	6.31±1.06	6.68±0.28	6.54±0.25
TS	1.07±0.5	0.39±0.1	0.52±0.1
VS	0.72±0.3	0.28±0.1	0.4±0.1
X: arithmetic average, S: standard deviation			

Table 3 General characteristics of treated wastewater (effluent)

Biological degradation of phenol in an activated sludge reactor

The figure 5 shows the behavior of the biomass during phenol degradation. The dark rhombus represent the volatile solids of mixed liquor from the aerobic reactor, which was inoculated with activated sludge from the Cerro de la Estrella municipal wastewater treatment plant in Mexico City, with a concentration of 12.6 g/L TS and 9.6 g/L of VS. During the first days of operation of the reactor, the biomass was acclimated to the phenol degradation of the industrial residual water with a phenol concentration of 0.48±0.025 g/L. However, once it starts with phenolic industrial wastewater feed with a phenol concentration of 2.81±0.35 g/L at an organic load of 11.2±0.3 KgCOD/m$^{3}\cdot$d, it is appreciated a substantial loss of biomass from the reactor. Behavior similar to that reported by Buitron et al (2005).

Aerobic granules can be formed in a wide range of organic loading, ranging from 2.5 to 15 KgCOD/m$^{3}\cdot$d, increased the size of the aerobic granules of 1.6 to 1.9 mm with organic loads of 3 to 9 Kg COD/m$^{3}\cdot$d (Liu et al., 2003a). So the physical characteristics of the aerobic granules depend on the loading speed, which may affect its morphology, density, specific gravity and volumetric index of sludge (VIS). In addition to high speeds of organic loading, it may occur a loss of integrity cell and by consequently, the disintegration of the granular structure (Liu et al., 2003b). Therefore, the behavior of the reactor biomass of activated sludges during their stabilization in contact with phenol, Is contrasted with that reported in the literature. However, from day 36 of operation and throughout the experiment, the biomass showed stable behavior to the extent that the organic load was reduced feeding, with an average concentration of volatile solids of the mixed liquor (VSML) of 1.9±0.36 g/L, sedimentability of 225±5 mL/775mL of supernatant, in an imhoff cone.

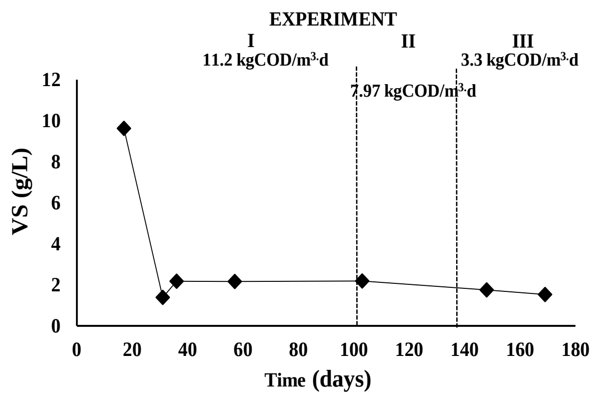

Figure 5 Variation of biomass with time

The figure 6 shows the profile of volatile solids (VS) in the influent and effluent of the reactor during the study to 1.76 days of HRT (experiments I - II) and 2.81 days of HRT (experiment III).

The clear rhombus represent the VS in the influent and the dark rhombu, the VS in the effluent and it is observed that at the moment of starting the feeding of the activated sludge reactor to higher organic load (experiment I), leads to a loss of biomass, due to the degree of phenol toxicity although that in a mixed culture activated sludge has a greater capacity of degradation of this type of toxic compounds, as the phenol (Shalaby, 2003). It has been reported that bacteria of the genus *Bacillus spp*., *Micrococcus spp*. y *Pseudomonas spp*. tolerate concentrations of 10 to 25 g/L of phenol (Yang et al., 2005). *Pseudomonas putida* with a capacity of degradation phenol of 500 to 600 mg/l in 48 hours of incubation. However, once the biomass has acclimated to the presence of phenol as the only source of carbon, was observed from the experiments II and III, a stable behavior, reaching average values 0.34±0.1 g/L. In this context, to avoid loss of biomass from the reactor, in addition to what is mentioned in the literature, on the factors involved in its biodegradation (Trigo, 2009), as temperature, pH, dissolved oxygen, substrate concentration, among others (Agarry, 2008).

As well as the organic loading speeds (Liu et al., 2003a). It is very important to have a biomass acclimatization strategy (Terreros et al., 2016). To allow the increase of the organic load, without affecting the metabolism, Nor the reproduction of the aerobic bacterial consortium, much less cause its cell death (Luo, 2009).

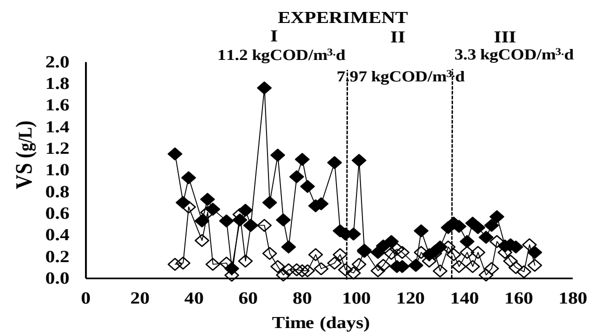

Figure 6 Variation of the concentration of solids with time

The figure 7 shows the performance of pH of the activated sludge reactor. The clear rhombus, represent the pH in the influent and the dark rhombus, the pH of the effluent. It can be seen that during the first 66 days of the experiment I, the pH of the reactor was very unstable reaching pH values of 5.56±0.79, which was probably due to the high organic load and to the toxic effect of the phenol on the bacterial population, perhaps causing the cellular death of a part of the initial biomass with which it was inoculated to the reactor when it was put into operation. And because organic matter is readily biodegradable, its availability as an easily biodegradable substrate caused the pH of the blended liquor to acidify. During the next days of operation, a tendency to rise to reach a mean value of pH of 6.93±1.06 (day 80 of operation). Finally, reach an average pH value of 6.31±1 at the end of this first run. During the experiments (II and III), the average pH values were of the order of 6.68±0.28 and 6.54±0.25 respectively. In response to the acclimatization of the biomass to the phenol of industrial wastewater with which it was fed to the activated sludge reactor throughout the experiment.

This allowed the experiment to proceed properly, without any inhibitory effect or disturbance affecting reactor performance during phenol biodegradation under the tested operating conditions.

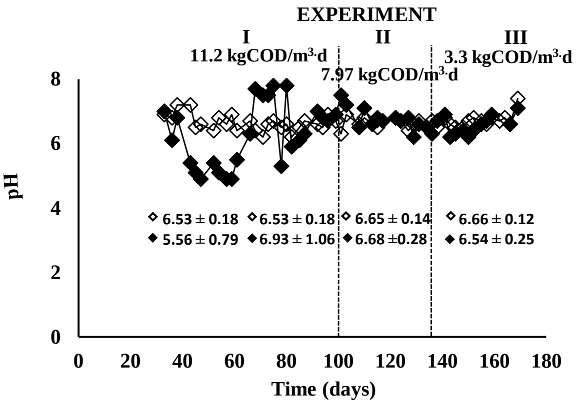

Figure 7 Variation of pH with time

In the figure 8, the efficiency of COD removal is shown, the clear rhombus represent the COD present in the influent and the dark rhombus, the COD in the effluent. It is observed that during the first 73 days of operation, due to the instability of the system, due to the phenol concentration of 2.81±0.35 g/L and organic load of 11.2±0.3 KgCOD/m^{3}·d (experiment I), The removal efficiency of COD was only 21%. However, as the biomass became acclimated to the presence of this toxic compound, an improvement in COD removal was observed in the last day of operation of this run, in a 51%. With the decrease of the organic load in 7.97±0.12 KgCOD/m^{3}·d, but higher phenol concentration (3.21±0.7 g/L) in the industrial residual water in the influent of the reactor (experiment II), a rate of COD removal of 62%. A significant change was observed in COD removal efficiency during the experiment III (34%) in which an organic load of 3.3±0.18 KgCOD/m^{3}·d was tested. The above may be explained as follows, that the biomass being exposed to the phenol of industrial wastewater, for a much longer time (HRT of 2.81 days), relative to the exposure time of the previous runs, its metabolic activity is Was affected, which is reflected in its ability to remove COD.

Because of its toxic nature, partial intoxication can result, and consequently partial loss of floc integrity and consequently the disintegration of its granular structure, thereby reducing its removal efficiency (Liu et al., 2003b).

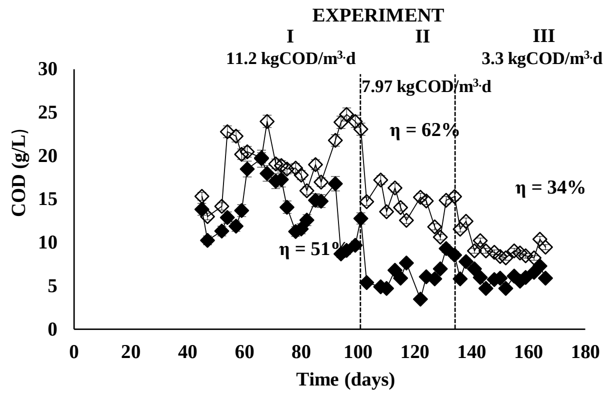

Figure 8 Variation of COD concentration with time

For his part, figure 9 shows the behavior of the reactor on the biodegradation of phenol, to a hydraulic retention time of 1.76 days (experiment I and II) and 2.81 days (experiment III) with an air flow of 2.5 L/min. The clear rhombus represent the phenol present in the influent and the dark rhombus, the phenol remaining in the reactor effluent. During the development of the experiment under the tested operating conditions, it was observed that as the organic load decreased from 11.2±0.3 to 3.3±0.18 KgCOD/m^{3}·d, the rate of phenol biodegradation also decreased. From 48% of phenol biodegradation in the first days of reactor operation, to only 29% phenol biodegradation, at the end of the experiment (experiment III). The decrease in the phenol biodegradation capacity of the mixed culture of the activated sludge reactor, given the toxic nature of phenol and the time of exposure of the bacterial consortium against this toxic compound (HRT of 2.81 days) in relation to that tested in the previous races.

I present the same effect discussed above, regarding the removal rate of COD, derived from the metabolic affectation of aerobic microorganisms, because of the toxic nature of phenol.

In this context, to achieve an adequate biodegradation of phenol present in industrial wastewater, it is necessary to use the best biomass acclimatization strategy (Terreros et al., 2016), as well as to make dilutions (Ba et al, 2014), in order to achieve its maximum rate of biodegradation, since it is reported in the literature that under aerobic respiration conditions, phenol can become a harmless compound because some aerobic bacteria use it as a source of carbon and energy (Ahmed et al, 2012). The phenol biodegradation results obtained in this study, under the proven operating conditions of the reactor, are in line with what has been reported in the literature. Since at low concentrations of phenol (250 mg/L), it results in 100% degradation. However, as the concentration increases (from 300 to 500 mg/L), the removal rate decreases by 94%, and for concentrations between 800 and 900 mg/L, the degradation profile decreases until reaching values of 93% (Busca et al, 2008), that is, at higher phenol concentration, lower rate of biodegradation.

While at concentrations of more than 1300 mg/L phenol, an inhibitory effect on the biomass is provoked and even, the total loss of the microbial activity can take place (Yoong et al, 2000). With these results, it is possible to treat industrial wastewater with phenol concentrations of 2.8 to 3.2 g/L and organic loading rates in a range of 7 to 11±0.2 Kg COD/m^{3}·d, at 1.76 days of HRT and 2.5 L/min of air.

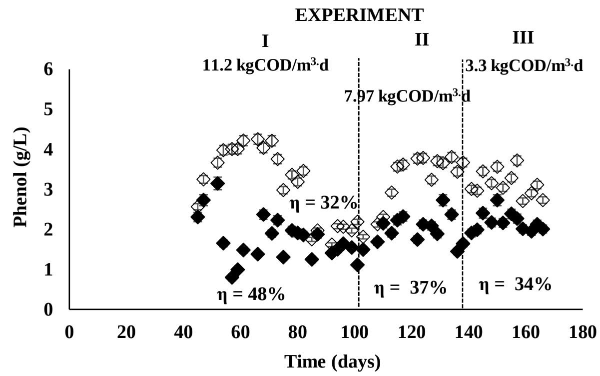

Figure 9 Variation of phenol concentration with time

Conclusions

The strategy used for the acclimatization of biomass from the biological reactor that was used in this research work, was a key factor in achieving biodegradation of phenol during the treatment of phenolic residual water of the resin industry. This allowed the reactor to perform adequately, without the need to use a co-substrate (glucose, fructose, etc), or to conduct encapsulation of the bacterial consortium, as mentioned in the literature, in spite of it, it was possible to biodegrade the phenol present in the wastewater, under the operating conditions of the reactor.

With the results obtained, is demonstrated, that it is possible to treat industrial wastewater with high concentrations of phenol, at high rates of organic load, in relation to the methods traditionally used for this purpose.

On the other hand, in addition to using the best strategy for the acclimatization of biomass, dilutions are recommended to reduce the effects of inhibition and intoxication of the bacterial population, in order to avoid any disturbance affecting the performance of the biological reactor and achieves, the maximum rate of biodegradation of this type of toxic compounds.

Solving in this way, a real problem of environmental pollution and human health, in addition to reducing the operating costs of the biological reactor during the achievement of said objective.

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Membrane receptors in glioblastoma cancer stem cells (GSCs)

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Abstract

Glioblastoma multiforme is the primary tumor most commonly diagnosed in the central nervous system, characterized by being highly angiogenic, proliferative, infiltrative and lethal. Resistance to chemo and radiotherapy further complicates treatment and offer a poor prognosis for the patient. This is due to the fact that it has a subpopulation called gliblastoma stem cells (GSCs), although several membrane proteins involved in the regulation of differentiated tumor cells of non-GSCs glioblastoma are known, there are new specific receptors that have been described in GSCs and the role they play in the origin, maintenance and progression of the disease by downstream regulation of self-renewal, undifferentiated state maintenance and proliferation.

Glioblastoma, GSC, CSC self-renewal, undifferentiation and proliferation

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Introduction

Glioblastoma multiforme (GBM) is a tumor type that originates from glial cells in the central nervous system (CNS) and is considered one of the most aggressive CNS tumors. When its ontogeny begins from a low-grade astrocytoma it is considered secondary glioblastoma, and glioblastomas that are generated from "novo" are called primaries. Although therapeutic management includes immunotherapy, chemotherapy, radiotherapy and surgical resection, the patient remains at mortal risk due to relapses.[1]

This is due to a subpopulation called glioma cancer stem cells (GSCs), which have membrane receptors distinct from differentiated glioma tumor cells. The α6β1, CD90, TfR1 / 2 TLR4, DRD4 and PTPRZ1 receptors play an essential role in chemo and radio resistance, and they also participate to regulate immune system evasion, self-renewal, undifferentiated state maintenance and cell proliferation. It is important to know the downstream signaling of these specific GSCs receptors to better understand the maintenance and expansion mechanisms of GSCs with a view to proposing new therapeutic targets.[2-4]

Primary GBM accounts for 16% of malignant neoplasms in CNS, tumor incidence increases on the basis of age, affects on average 7.2 people per 100,000 adults (> 19) per year; the diagnosis in people aged 75-84 years has an annual incidence of 14.6 people per 100,000 and in children (age <19) to 0.8 per 100,000.[5] In Mexico there is no specific registry of primary neoplasms originating in the CNS. However, reports by GLOBOCAN on primary tumors that originate in the CNS, the incidence comprises 2,998 neoplasias, which is equivalent to 2.3% of malignant tumors.[6]

Cancer stem cells (CSCs)

Cancerous trocal cells were first isolated in 1994 by Bonnet and Dick et. al., being isolated from acute myeloid leukemia. The maintenance of undifferentiated state, self-renewal and proliferation of CSCs is mediated by a number of molecules including membrane receptors that regulate downstream signaling pathways linked to the activation of cell cycle regulatory genes, undifferentiation and Warburg effect. In addition, CSCs increase their survival and mitotic activity in hypoxic environments through the HIF-1α and HIF-2α proteins (Hypoxia-induced Factors 1 and 2). However, master receptors that play a key role in maintaining trunkiness are Notch, LRP5 / 6 (Low Density Lipoprotein 5 and 6 Receptor), FDZ5 (Receptor Fridzzled 5), CD133 (Cluster Differentiation 133) , Thy-1 or CD90 (Cluster of differentiation 90), EpCAM (epithelial cell adhesion molecule) and ABC Transporters.[7-18] The WNT ligand mediates the activation of one of the most important pathways in CSCs, the β-catenin / GS3K pathway in CSCs. In non-cancerous stem cells (non-CSCs), β-catenin is phosphorylated and polyubiquitinated subsequently to be sent to 20S proteasome degradation, this mechanism is orchestrated by a protein complex called "destructive complex" that has the activity of Axina, APC (adenomatous polyposis coli), GSK3β (glycogen synthase kinase 3β) and CKIα (casein kinase Iα).[19-20]

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In addition, cytoplasmic proteins such as aldehyde dehydrogenase, BCL2, γ-secretase, JNK (c-Jun N-terminal), STAT3 (signal transducer and transcription activator 3), PKCα (Protein cyanase C alpha), PLCγ phospholipase C-γ) and Smad4, which at the intracellular level play an important role in the activation of genes logged to the trunk, proliferation and survival. In addition, they have the expression of the factors of Yamanaka Oct-4 (Transcription Factor to Octamer 4), Sox2 (Sex Determining Region Y) - Klf4 (Kruppel-like Factor 4), Nanog of transcription Homeobox NANOG) and c-Myc (Viral Avian Myelocitomatosis Oncogen Homologus), which are indispensable for maintaining cell undifferentiation and a pluripotent state.[21-23]

Cancerous stem cells in glioblastoma (GSCs)

They were described in 2002 by Ignatova et. *al.* In addition, GSCs represent between 0.5% and 0.1% of the tumor mass in tumors obtained by surgical resection and 10% from primary cultures supplemented for the maintenance of truncation and pluripotency. They have the characteristic truncated surface receptors such as Notch, Shh, WNT and CD133 and also present the β-catenin / GS3K pathway in GSCs.[24-28] The key role of the CD133 receptor in chemoresistance has been demonstrated in in vitro assays because it downstream regulates the PI3K / AKT pathway (Phosphatidylinositol 3 kinase / Protein Kinase B).

PI3K phosphorylates the AKT protein in T308 and DNA-PKcs phosphorylates S437 by promoting AKT-mediated IKKα (Kappa-B subunit kinase inhibitor) phosphorylation. Phosphorylation in IKKα interacts with IκB (Nuclear Factor Inhibitor Kappa-B subunit alpha kinase), phosphorylated IκB breaks its interaction with the IκB / NF-κB complex (nuclear factor kappa B) by freeing NF-κB in its active form, is translocated to the nucleus by interacting with the promoter of the MDR1 (Multiple Drug Resistance Protein 1) gene, which promotes its transcription into non-GSCs.[29-32] Although the activity of these receptors in non-GSCs is known, novel GSCs-specific receptors have also been described that also have tumorigenic activity such as radio resistance and chemotherapy. However, they not only confer these qualities, they also participate in mediating the survival, migration, dedifferentiation, self-renewal and proliferation GSCs.[33] Table 1 shows the main receptors of glioblastoma cancer stem cells and their location in two databases, to expand information.

Integrin alpha 6 subunit (ITGA6)

The membrane protein ITGA6 also known as α6β1, is overexpressed in astrocytoma, meningioma, neuroblastoma and glioblastoma, as opposed to healthy brain tissue.[34] However, its presence has been demonstrated in the subventricular zone (SVZ); this region of the brain is very important because it carries out embryonic and postnatal neurogenesis. This has led to the generation of the hypothesis about the possible site of origin of the GSCs.[35-36] Ligands interacting with ITGA6 are laminins and other extracellular matrix molecules. The presence of ITGA6 in GSCs was demonstrated in 2010 by Justin D.

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Lathia *et. al*. who determined that ITGA6 can be found concomitantly in cells with CD133 (+) and CD133 (-), in addition, by siRNA directed to ITGA6 determined that the silencing of it, compromised the auto-renewal and cellular motility of GSCs.[37] The ITGA6 protein is indispensable for the increase of proliferation and decrease of apoptosis in vitro and in vivo in glioblastoma, the silencing of ITGA6 allows for apoptosis in GSCs regulated by TNFα / TNF-R1 (Tumor Necrosis Factor alpha / Factor Receptor tumor necrosis 1), downstream activating the p38MAP / JNK pathway (38 / c-Jun N-terminal mitogen-activated protein kinase); and the inhibition of apoptosis is mediated by cFLIP (protein cell inhibitor of FLICE) is activated upstream by ITGA6, as high levels of cFLIP inhibit caspase-8 (apoptosis 8-related protein peptidase) which forms part of DISC (death-inducing signaling complex). In addition, ITGA6 increases in perivascular areas and regulates tumor migration by the downstream activation of laminin-111 and the anti-coagulation factor VIII, enhancing its angiogenic, proliferative and invasive capacity.[38-41] UniProt: P23229

Thy-1 cell surface antigen (THY1)

This protein is also known as CD90; was identified by tissue microarrays, analyzing varying degrees of tumor, CD90 expression was significantly higher in high grade tumors. Cells bearing CD90 (+) also co-expressed CD133 (+).[42] CD90 levels were highly expressed in GSCs but not the same in differentiated tumor cells, the self-renewal assay was performed to observe whether CD90 was in GSCs, CD90 (+) / CD133 (+) cell population required an equal amount of cells for the formation of neurospheres compared to CD90 (-) / CD133 (+) cells which required up to twice as much cell volume to form neurospheres and self-renewal.

CD90 is co-localized with CD31 in endothelial cells lining the tumor vasculature creating an angiogenic niche favoring the production of Notch by paracrine regulation of self-renewal of GSCs.[43-46] UniProt: P04216

Receptors 1 (TFRC) and Transferrin 2 (TFR2) and Ferritin Light Chain (FTL)

TFCR and TFR2 receptors are known as TfR1 / TfR2, and are commonly expressed in glioblastoma both in vitro and in vivo; are activated by interacting with Fe^{2+} and transferrin particles.[47] TFRC plays an important role in the chemoresistance and as surface marker of GSCs was determined by Mi Kyung et. al.[48] TFRC levels are high in GSCs, being activated induces the synthesis of FTH1 (Ferritin heavy chain 1) and FTL (light ferritin chain). FTL interacts with FTH1 and handles the processing and catabolism of the Fe^{2+}. It regulates downstream the STAT3 pathway, which phosphorylates FoxM1 (M1 Fork Box), favoring cell cycle activation in CSCs and GSCs. The presence of FoxM1 is regulated positively in different types of cancer and is also highly expressed in GSCs; also interacts with c-Myc enhancing cell proliferation, in GSCs. The STAT3 and FoxM1 proteins appear to be dependent on ferritin receptors, since the inhibition of TFRC promotes the generation of free radicals and reactive oxygen species that trigger the response of the antioxidant response elements (AREs). When the active AREs repress the activity of the ferritin, however, this is neutralized by the PIAS3 (E3 sumo-protein ligase) a protein repressor of STAT3 this generates a loop of self-regulation, in addition, TFRC compromises the proliferation, self- renewal and promotes the differentiation of GSCs both in vitro and in vivo and decreases their ability to form tumors in xenotransplants.[49-53]

TFR2 promotes resistance to temozolomide since the silencing of TFR2 sensitizes the cells treated in culture with temozolomide, in addition, it activates downstream the ERK1 / ERK2 pathway (Kinase related to extracellular signaling 1 and 2) which is overexpressed in GBM and GSCs.[54, 55] UniProt: P02786; Q9UP52; P02792.

Protein tyrosine phosphatase Z1 receptor (PTPRZ1)

It was described during a microarray analysis in glioblastoma and differences between the expression levels of differentiated cells and GSCs were identified; the presence of the protein was corroborated by western blotting.[56-57] The PTPRZ1 receptor is highly expressed in glial progenitors and is responsible for regulating self-renewal.[58-59] M2 (type 2 macrophages) and TAMs (tumor associated macrophages) secrete PTN (pleotrophin) to stimulate GSCs through interaction with PTPRZ1. The PTPRZ1 protein mediates activation downstream of PI3K / AKT by promoting phosphorylation of serine 437 in AKT and phosphorylation in tyr 416 in Src cyanase, which belongs to the SFK (Src kinase family). The phosphorylation of AKT is carried out by Fyn kinase (FYN tyrosine protein cyanase) and Src (V-Src Avian sarcoma) are at the same time phosphorylated when the upstream signal is induced by PTPRZ1 because they share the same site of phosphorylation in Tyr416, its inhibition compromises the pluripotent state, proliferation and self-renewal.[60-65] UniProt: P23471

Toll-like receptor 4 (TLR4)

TLR4 is highly expressed in neuronal stem cells (NPCs), the absence of the TLR4 receptor potentiates neuronal differentiation and proliferation.[66-67] In GSCs TLR4 is inactive, because high levels of TLR4 inhibit proliferation; the decrease of TLR4 allows the maintenance of undifferentiated state and self-renewal. The TLR4 receptor mediates downstream phosphorylation of TBK1 (serine / threonine protein kinase 1) and interacts with RBBP5 (retinoblastoma binding protein 5) which inhibits its activity, thereby reducing the mRNA levels of SOX2, OCT4 and NANOG . The absence of TLR4 is vital for the maintenance of GSCs, proliferation and self-renewal, by activating the retinoblastoma binding protein 5 (RBBP5) that interacts with MLL1 (myeloid / lymphoid or mixed lineage leukemia) that is part of the protein complex WRAD (Romano-Ward Syndrome) and can modify the epigenome in GSCs. Alterations in MLL1 affect the epigenetic state in the promoter regions of the pluripotency genes SOX2, OCT-4, NANOG, where the methylation marks associated with the lysine 4-mediated transcriptional activation of $H3_{me}^{3}$ (histone 3 trimethylated).[68] UnitProt: O00206.

Dopamine D4 Receptor (DRD4)

The DRD4 receptor has recently been reported in glioblastoma and plays an important role in clonogenic potentiation. The DRD4 gene is not methylated in glioblastoma; however, inhibition of methylation favors the therapeutic efficacy of temozolomide in patients with GM. It reduces levels of adenylate cyclase and inhibits cAMP (cyclic AMP). Cells treated with DRD4 antagonists carry genes involved in DNA replication, cell cycle, and on the contrary, genes related to autophagy are activated.

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It also increases the expression of genes involved in lipid biosynthesis. DRD4 antagonists increase the synthesis of LC3-1 / 2 (light chain proteins associated with 1/2 microtubules), which are markers of the autophagosome. They also increase p62 (nucleosporin) and LAMP1 (lysosome-associated membrane protein), both of which are key regulatory proteins for autophagy. The PDGFRβ-ERK1 / 2 signaling pathway (Factor Receptor derived from beta platelets and kinase related to extracellular signaling 1 and 2) is transactivated by DRD4, so the inhibition of DRD4 affects the phosphorylation of S6 in mTOR which leads to the induction of caspases 6/7 (apoptosis-related peptidase protein 6 and 7), cell cycle arrest followed by apoptosis.[69-70] UniProt: P21917

Receptor	Function	Ligands	Reference	UniProt[71]	neXtProt[72, 73]
ITGA6	Self-renewal, proliferation, cell motility, angiogenesis, anti-apoptotic and biomarker.	Laminin-111 and extracellular matrix components.	37	P23229	NX_P23229
THY1	Self-renewal, biomarker, angiogenesis.	CD45 (Cluster of differentiation 45)	42	P04216	NX_P04216
TFRC1	Activation of the cell cycle, self-renewal, proliferation, undifferentiation, biomarker.	Fe^{3+} and Transferrin	47	P02786	NX_P02786
TFRC2	Biomarker, chemoresistance, activation of the ERK1/2 pathway.	Fe^{3+} and Transferrin	48, 55, 57	Q9UP52	NX_Q9UP52
PTPRZ1	Self-renewal, undifferentiation, proliferation.	Pleotrophin.	60, 61,62	P23471	NX_P23471
TLR4	Self-renewal, proliferation, undifferentiation and activation of genes linked to pluripotency.	Absence of the receptor in GSCs.	69	O00206	NX_O00206
DRD4	Inhibition of autophagy, proliferation, undifferentiation, anti-apoptotic, transactivation of the PDGFRβ-ERK1/2 pathway, activation of mTOR.	Dopamine.	71	P21917	NX_P21917

Table 1 Principal recipients of glioblastoma cancer stem cells

Conclusion

Stem cells or glioma stem cells, GSCs, are capable of self-renewing in culture, and give rise to neurons and glia both in vivo and in vitro. Therefore, they are considered multipotential cells whose function is tissue replacement and regeneration; that for it to be carried out effectively requires complex processes involving targeted migration and growth that ensure connections at a distance.

Knowing the receptors described so far in the glioma stem cells allow to better describe the mechanisms involved in the origin, maintenance and progression of the disease, as shown in Figure 1; with the inherent unveiling of new therapeutic targets. This is a brief description of the main receptors of GSC, which allows the reader to have a first approach with these molecules and prepares them to delve into the molecular processes that are mediated by receptors of glioblastoma cancer stem cells.

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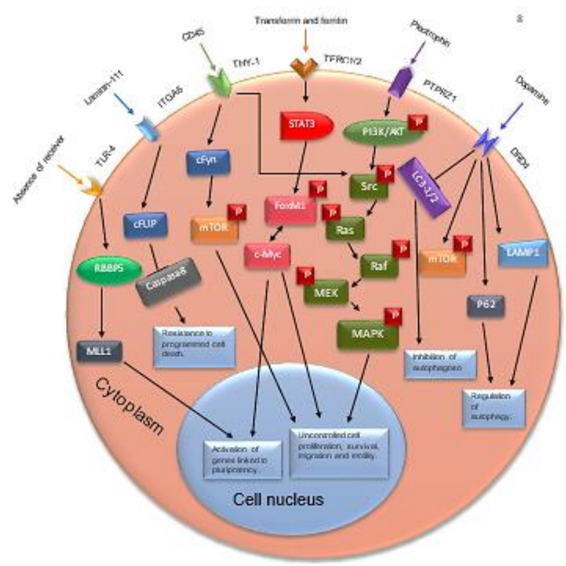

Figure 1 Scheme of GSCs with different membrane receptors, ligand and transduction of signals that exert downstream and at cytoplasmic and nuclear level

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Risks of cerebral vascular disease in teachers and university employees

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Abstract

Noncommunicable diseases, commonly known as non-chronic or lifestyle-related diseases are cardiovascular diseases, diabetes, cancer and chronic respiratory diseases, which cause almost 80% of the deaths attributable to them. Objective. To determine the risks of Cerebral Vascular Disease in Teachers and University Employees. Methodology. Non-experimental, descriptive and transectional study. The sample was made up of 225 professors and university employees. A non-probabilistic sampling was done for convenience. An instrument was designed that, when piloting, obtained an acceptable reliability with Cronbach's alpha of 0.690, structured in three sections with dichotomous questions. Contribution. It will enable the institution to implement strategies aimed at promoting healthy lifestyles among academic staff and employees. With the adoption of healthy behaviors will promote the prevention of noncommunicable diseases that in future represent high costs to the health services and the institution due to the temporary and / or permanent incapacities that, if condition present.

Hypertension, Diabetes, Cancer

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Introduction

Cerebrovascular disease (CVD) is a clinical syndrome characterized by rapid development of focal neurological signs, which persist for more than 24 hours. No other apparent cause than vascular origin. It is classified into two subtypes, ischemia and hemorrhage. (Arauz, 2012). According to WHO, CVD is a public health problem and is the second leading cause of death in low- and middle-income countries. If no effective interventions are made by 2030 it will increase to 44%. According to the Secretary of Health, in Mexico since 2000 to date mortality for this cause has increased.

Health situation in Michoacán reflects a complex scenario, changes in demographic structure, as well as in habits and lifestyles, have generated changes in the epidemiological profiles of the population, combat historical problems such as infant mortality, maternal mortality, transmission by infectious diseases and, on the other hand, to prevent and treat noncommunicable diseases derived from the aging of the population and an unhealthy lifestyle.

The Michoacan University of San Nicolás de Hidalgo has a teaching staff of about 3500 teachers and about 3000 employees. In both cases, risk behaviors have been observed for cardiovascular and endocrine diseases, because problems have been identified with lack of physical activity, consumption of tobacco, stress and food, with respect to the latter, people are not in the habit of taking food from their homes and regularly buy it in places where fast food is sold. It is common for employees to take half an hour to eat food, and these are not always healthy, if they are considered to be regularly purchased near their work center.

These consist of coffee with cookies or bread, cakes, tacos, toast, baguettes, fruit, among others. In addition to the consumption of food with low nutritional value such as churros, fries and sweets. Therefore, this research was done with the objective of determining the risks of cerebral vascular disease in university professors and employees. This will allow the search for institutional strategies to promote healthy behaviors and eliminate or reduce risk behaviors in order to prevent future health problems that condition temporary or permanent disabilities, especially if we consider that it is a young population that in the future would imply for the institution and the society greater expenditures on health.

Epidemiological data

In 2011, world leaders, recognizing the devastating impact of NTD (non-transmitted diseases), adopted a policy with firm commitments and entrusted WHO with supporting the efforts of countries, through the development of a Global Plan of Action for prevention and control of non-transmitted diseases 2013-2020 (known as the WHO Global Plan of Action on NTD), this includes nine global targets for voluntary implementation and a global monitoring framework. These were adopted by the World Health Assembly in 2013. (WHO. 2016).

It is important that countries give priority to interventions aimed at reducing the harmful use of alcohol, insufficient physical activity, salt or sodium intake, smoking and hypertension; halt the rise in obesity and diabetes, and improve treatment coverage to prevent heart attacks and strokes, and access to basic technologies and medicines (Who's Report, 2014).

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NTDs are the leading cause of death in the world, causing 38 million (68%) of the 56 million deaths recorded in 2012. More than 40% (16 million) were premature deaths occurring before age 70 old. Nearly three quarters of all NTD deaths (28 million) and most of the preterm deaths (82%) were in low- and middle-income countries. For the period 2011-2025, the cumulative economic losses in these countries in the hypothesis of maintaining the current situation, are estimated at US $ 7 trillion. This huge cost of inaction far outweighs the annual cost of implementing a set of strong impact interventions to reduce NTD burden ($ 11.2 billion per year). (WHO, 2014)

At present, Mexico and the United States, are the first place of world prevalence of obesity in the adult population (30%). (Barrera, 2013). According to INEGI in 2015, the 10 main causes of mortality in Mexico were heart disease (ischemic heart disease), diabetes mellitus, malignant tumors, accidents (motor vehicle traffic), diseases of the liver (alcoholic liver), cerebrovascular diseases (CVD), chronic obstructive pulmonary diseases, aggressions, influenza and pneumonia, and renal failure.

At the national level, cerebrovascular diseases ranked fourth in women and seventh in men. In 2011, in the State of Michoacán, diabetes mellitus, ischemic heart diseases, cerebrovascular diseases and lower respiratory tract chronicles were the main causes of death in the population; these caused 35.8% of the total deaths. (Health Secretary, 2014).

By 2015 in the state of Michoacán, CVDs ranked fifth as causes of mortality and according to sex, in men aged 45-64 years was found in seventh place and fifth place in women. It should be mentioned that according to the main results of the Intercensal Survey 2015, the State of Michoacán is among those that do not reach 80% of its population affiliated to an institution that offers health care services, however, this condition should not affect teachers and university employees because a social benefit is the affiliation to the Mexican social Security Institute (IMSS), in the case of teachers, provided they impart the number of hours required to apply the provision.

Lifestyle

Lifestyle is a construction of the individual, molded by family, education and society. In epidemiology the term lifestyle is understood as a set of behaviors that people develop, which are sometimes healthy and others are harmful to health. (Cited by Guerrero, 2010)

Among the eating habits associated with weight gain is eating out frequently. Also eating at restaurants and places that sell fast food impacts negatively on the health of people. The dietary habits of the countries of Latin America are related to the sociodemographic, economic and dietary changes that the population has had.

This results in increased consumption of foods rich in saturated fats, cholesterol, sugars, refined flours and sodium among others. Bringing as a consequence the increase in chronic non-transmitted diseases and obesity (Schnettler, 2013).

Healthy lifestyles promote the acquisition and maintenance of individual and collective behavior patterns that improve the quality of life: it includes behavior patterns, beliefs, knowledge, habits and actions of people to maintain, restore or improve their health, well-being and quality of life. The well-being of people is associated with their diet, sociodemographic characteristics, preferences for certain foods with a good health and with the pleasure associated with food. (Schnettler, 2013).

Non-transmitted diseases (NTDs) represent one of the greatest challenges of the 21st century for health and development, both for the human suffering they cause and for the harm they cause to the socio-economic fabric of countries, especially those of low and medium income. Non-transmitted diseases, commonly known as non-chronic or lifestyle-related diseases are cardiovascular diseases, diabetes, cancer and chronic respiratory diseases, these cause almost 80% of the deaths attributable to these diseases. They share four major risk factors, including tobacco use, poor diet, sedentary lifestyle, and harmful use of alcohol. These diseases represent an important burden in low- and middle-income countries.

The highest increase in the prevalence of obesity between 1999 and 2006 was observed in the indigenous population (<15% per year). These trends suggest that Mexico is carrying an excessively heavy burden of weight for the poorest population at all ages.

The patterns of consumption in Mexican households between 1992 and 2010 are different according to income level. Households with lower income decide on spending that allow them to consume a higher level of calories at a lower price, but of lower nutritional quality. (Rivera, 2012).

The evaluation of nutritional status in adults aged 20 years and over showed a prevalence of overweight and obesity by sex, 74.6% in women and 70.2% in men, with a Body Mass Index greater than or equal to 30kg / m2. It was 48.9% and 36.8%, respectively. In the last six years the prevalence increased 2.4% in men and 3.8 in women. (State Strategy. 2015)

Cardiovascular risk factors

Cardiovascular risk factors (CVRF) associated with CVD include those of a non-modifiable type such as: age, gender, family history, race and other modifiable ones, susceptible to therapeutic intervention such as systemic arterial hypertension (SAH), coronary artery disease, dyslipidemia, diabetes mellitus (DM) and smoking, among others. Both relative (RR) and attributable (AR) risk are very high. (Rodríguez, 2010). The most important predictor of fatal event is the pulse pressure which is an indicator of hardening of the aorta. (Alcalá, 2010)

Unplanned urbanization, the aging of the population, the globalization of trade and products, especially tobacco, alcohol and food, have led to an increase in risk factors. Lack of capacity to provide medical care and social protection systems increases the risk of contracting diseases and the person dies at an earlier age (United Nations General Assembly Report, 2011).

The main risk factors for mortality from diseases such as diabetes mellitus, ischemic heart disease and cerebrovascular disease were overweight and obesity, high blood glucose concentrations, alcohol consumption and smoking, solely obesity and high glucose explained 25.3% of the total deaths in the country (Rivera, 2012).

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With regard to age, it has been estimated that for every decade after 55 years the risk of CVD is doubled. Some authors point to another factor that can not be modified race or ethnicity, based on the great differences between African Americans, US Indians, Hispanics and the white population, especially among those under 65 years of age.

Smoking represents a Relative Risk (RR) of 1.8 for CVD. Likewise, diabetes mellitus, since it is a risk factor that in turn produces macrovascular changes that result in hypertension. Asymptomatic carotid stenosis, which increases the risk of CVD in a manner proportional to the degree of obstruction of the affected artery, although when there are almost total degrees of obstruction and the RR does not increase anymore. (Alcalá, 2010).

To avoid the most important modifiable risk factors there are two levels; to prevent the occurrence of risk factors for cardiovascular disease (obesity, smoking, physical inactivity) and to treat diseases such as hypertension, considered as a special risk factor. (Alcalá, 2007). The DASH diet (Dietary Approach to Stop Hypertension) includes eight types of food: fruits, vegetables, cereals, nuts, legumes, low-fat dairy products, few red meats processed and low sugar and sodium drinks (Ruiz, 2010).

According to the body mass index (BMI), it is considered overweight when it is 25 to 29.9 and obesity when it is ≥ 30. In relation to the waist circumference (WC), abdominal obesity according to the International Diabetes Federation (IDF) occurs when the WC is greater than 90 cm in men and 80 cm in women. The WC is measured with a flexible tape measure in the middle between the costal border and the iliac crest.

The patient should inhale and then remove all the air a couple of times and thus obtain the measurement. In our country the prevalence of overweight and obesity is 70% according to BMI, while 84% of women and 64% of men have abdominal obesity according to the definition above.

Sedentary lifestyle and physical exercise are two factors that have an impact on the risk of CVD, lifestyle changes have led people to lead a sedentary life, that is, they remain for a long time sitting or not moving, whose situation conditions problems of overweight and / or obesity. A meta-analysis of 18 studies showed a decreased risk of CVD or death of 27% if intense physical activity was performed well before the event (RR: 0.73; 95% CI 0.67 to 0.79, $p < 0.001$) compared with the activity light physics. The risk reduction for HF was 21% (RR: 0.79; 95% CI 0.69 to 0.91, $p < 0.001$) and for ICH 34% (RR: 0.66; 95% CI 0.48 to 0.91, $p < 0.001$). the Framingham Registries, the Olso Study and the Nurses Health Study of Copenhagen have shown that physical exercise reduces the risk of premature death and cardio and cerebrovascular disease in men as well as in women. (Ruiz, 2010)

In 2014, the WHO in the Report on the World Situation of the Prevention and Control of NTDs establishes nine global goals, listed below, taking into account that each one identifies risk factors for NTD as the CVD:

Global target 1: Relative reduction of overall mortality from cardiovascular diseases, cancer, diabetes or chronic respiratory diseases by 25% by 2025.

Global target 3; relative reduction of the prevalence of insufficient physical activity by 10% by 2025. Insufficient physical activity contributes to causes the loss of 69.3% million DALYs and 3.2 million deaths each year.

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The risk of death from any cause is higher in adults whose physical activity is insufficient than in those who practice at least 150 minutes of moderate physical exercise per week or its equivalent as recommended by the WHO. Regular physical activity reduces the risk of ischemic heart disease, stroke, diabetes, and breast and colon cancer.

By 2014, 23 per cent of adults aged 18 and over were not active enough, women were less active than men and older people were less active than young men. In recent years, more low- and middle-income countries have established initiatives to address the problem of physical inactivity. Achieving this goal requires the multisectoral collaboration of the departments of transportation, urban planning, recreation, sports and education, in order to create safe environments conducive to physical activity for all age groups.

Global target 4: Relative reduction in average salt or sodium intake by 30% by 2025. Excessive consumption of sodium in the diet has been associated with an increased risk of hypertension and cardiovascular disease. Globally, 1.65 million deaths annually from cardiovascular causes have been attributed to an excessive sodium intake. The average worldwide intake of salt is of the order of 10 g daily (3.95 g / day of sodium).

The WHO recommends a reduction in salt intake of less than 5g / day (2 g / day of sodium) to reduce blood pressure and the risk of coronary heart disease and stroke.

In some countries, the main source of salt is processed foods and precooked foods, while in others salt is added during food preparation at home and at the table. It is worth mentioning that by increasing the availability of processed foods, they quickly become the main source of sodium.

Global target 5: Relative reduction in the prevalence of current tobacco use by 30% for people aged 15 years or more by 2025. An estimated six million people are currently dying from tobacco use, including more than 600,000 deaths due to exposure to foreign smoke, of which 170 000 are children. The measures for reduction are: to protect people from exposure to second-hand smoke through national legislation on "100% smoke-free environments"; offer help to quit smoking, and warn people about the dangers of smoking.

Global target 6: Relative reduction in the prevalence of hypertension by 25% to contain the prevalence of hypertension, depending on the circumstances of the country by 2025. It is estimated that hypertension has caused 9.4 million deaths and 7% of the burden of morbidity -expressed in DALY- in 2010. Uncontrolled hypertension is a cause of stroke, myocardial infarction, heart failure, dementia, renal failure and blindness. The global prevalence of hypertension (defined as systolic and / or diastolic blood pressure equal to or greater than 140/90 mmHg) in adults 18 years of age or older was 22% in 2014.

The modifiable factors are: consumption of foods that contain too much salt or fat, insufficient intake of fruits and vegetables, overweight and obesity, harmful use of alcohol, physical inactivity, psychological stress, socioeconomic determinants and access inadequate to health care. At the global level, detection, treatment and control are insufficient because of the precariousness of health systems, particularly at the primary care level. (Report 2014. Page IX). Establish comprehensive programs at the primary care level to enhance the effectiveness of screening, diagnosis and treatment.

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Global target 7; detection of increased diabetes and obesity by 2025. Obesity increases the likelihood of diabetes, hypertension, coronary heart disease, stroke and certain cancers. Globally, obesity has almost doubled since 1980. By 2014, 10% of men and 14% of women aged 18 and over were obese. The global prevalence of diabetes in 2014 was estimated at 10%. Obesity and diabetes can be prevented through multisectoral action that contributes to the production, distribution and marketing of food and creating environments that facilitate and promote physical activity. The risk of diabetes can be reduced by moderate weight loss and moderate daily physical activity.

Global target 8. Pharmacological treatment and counseling (including blood glucose control) for at least 50% of people who need it to prevent heart attacks and strokes by 2025.

Cardiovascular diseases were the leading cause of death by NTD in 2012 and were responsible for 17.5 million deaths, or 46% of deaths from NCDs. An estimated 7.4% were due to heart attacks (ischemic heart disease) and 6.7 million to strokes.

An intervention that can be carried out at the primary care level is the improvement of the coverage of pharmacological treatment and the counseling of people exposed to a high cardiovascular risk or who already suffer from the disease.

Since 1980, obesity has doubled around the world. By 2014, more than 1900 million adults aged 18 and over were overweight, of whom more than 600 million were obese. By 2014, 39% of adults aged 18 and over were overweight and 13% were obese. Most of the world's population lives in countries where overweight and obesity charge more people's lives than underweight. Being overweight and obese, they are defined as an abnormal or excessive accumulation of fat that can be harmful to health.

The Body Mass Index (BMI) is a simple indicator of the relationship between weight and height that is frequently used to identify overweight and obesity in adults.

In adults, the WHO defines overweight and obesity as: overweight: BMI equal to or greater than 25. Obesity equal to or greater than 30.

BMI provides the most useful measure of overweight and obesity in the population, since it is the same for both sexes and for adults of all ages. However, it should be considered as an approximate value because it can not match the same level of thickness in different people. A high BMI is an important risk factor for noncommunicable diseases such as:

Cardiovascular diseases (heart disease and cardiovascular accidents) that were the leading cause of death in 2012.

Diabetes. Disorders of the locomotor system (especially osteoarthritis, a degenerative joint disease and very disabling), and some cancers (endometrium, breast, ovaries, prostate, liver, gallbladder, kidneys and colon). The risk of contracting these non-transmitted diseases grows with increasing BMI.

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Overweight and obesity can be prevented when people choose to: limit the energy intake that comes from the amount of total fat and sugars, increase consumption of fruits and vegetables, as well as pulses and whole grains and nuts; and regular physical activity (60 minutes a day for young people and 150 minutes a week for adults). Individual responsibility is fundamental to having an effect on a healthy way of life. It is therefore essential to consider what the NOM 043 establishes.

Obesity (BMI $\geq$30kg/m^2) is a systemic, chronic and multi-causal disease, not exclusive to economically developed countries, involving all age groups, of different ethnicities and social classes. It has reached epidemic proportions worldwide, which is why the World Health Organization (WHO) has called it the epidemic of the 21st century (Davila, 2015). According to the (WHO) obesity is the most frequent non transmitted chronic disease. The WHO defines overweight and obesity as an abnormal or excessive accumulation of fat. In addition, there is evidence that this condition is the main risk factor for the development of chronic nontransmitted diseases, it is estimated that 90% of type 2 diabetes mellitus are attributable to overweight and obesity, as well as cardiovascular diseases, disorders of the locomotor system (osteoarthritis) (IMCO, 2015) and is associated with an increased risk of endometrial, esophagic, renal, pacritic, ovarian, breast, colorectal, thyroid and gallbladder cancer.

It is also associated with leukemia, multiple myeloma, non-Hodgkin's lymphoma, and multiple melanoma. (Mitchel, 2011).

In Michoacán, seven out of ten people are involved with one or more of the diseases such as diabetes, overweight or obesity. (Secretary of Health, 2014).

Considering the above, the following question was raised:

What are the risks of stroke in college teachers and employees?

Objectives

General

To determine the risks of cerebral vascular disease in university professors and university employees.

Specifics

Identify risk factors for stroke in teachers and employees.

Relate risk factors for stroke among teachers and university employees.

Methodology

Non-experimental, descriptive, transectional and exploratory study. The study population was composed of teachers and university employees. A non-probabilistic sampling was done, at the convenience.

We included 225 professors and employees assigned to the university units of Morelia, Michoacán, excluding those who did not wish to do so and those enrolled in the campuses outside Morelia. After informed consent, a structured instrument was applied in four sections that was validated with a Cronbach Alpha of 0.729. Being an instrument with an acceptable reliability. Anthropometric measures such as weight, height, hip circumference, wrist circumference, BMI and ICC were taken.

Also, blood pressure was measured, with an aneroid baumanometer of the brand WelchAllin (German), bracelet of 25 to 34 or 32 to 43cms, these were changed according to the complexion of the participant. The measurement was made with the person sitting in a backed chair, not having ingested coffee, not having performed physical activity, or having climbed stairs 30 minutes prior to the intake, according to NOM 030. A sample was taken of peripheral blood to measure glucose, cholesterol and triglycerides. A sterile lancet was punctured and a test strip was used for each of the parameters to be measured. The apparatus used for this was the Accutrend Plus Cobas (German). The participant should be fasting for at least 8 hours. Stature was measured using a digital scale and BMI was calculated. The research was done in accordance with the health research guidelines and the Helsinky Declaration.

Results

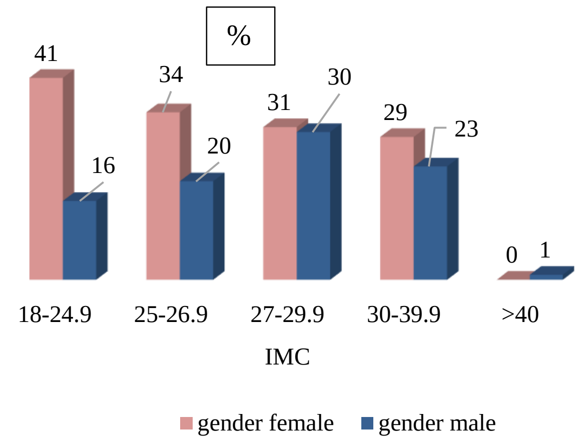
According to the analysis, the following results were obtained:

60% (135) of the respondents were women and 40% (90) men. The Ẋ of the height was of 162.8 mts and weight 72.0 kgs.

Age	**Frecuency**	**%**
26 - 31 y/o	28	12.4
32 - 37 y/o	45	20.0
38 - 43 y/o	47	20.9
44 - 49 y/o	49	21.8
50 y/o or more	56	24.9
Total	225	100.0

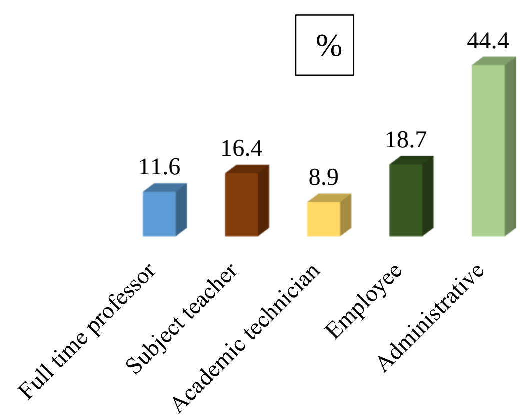
Table 1 Age of teachers and employees. Morelia. 2017
Source: 225 Questionnaires applied to teachers and employees

The Ẋ age was 43 years, 24.9% were 50 and over, 21.8% were 44 - 49 years old. The rest of the respondents are shown in table 1.



Graphic 1 Sex and BMI of teachers and employees
Source: 225 Questionnaires applied to teachers and employees

Regarding gender and BMI, a greater number of women with above normal BMI parameters were found in relation to men.



Graphic 2 Category of participants. Morelia, 2017
Source: 225 Questionnaires applied to teachers and employees

Of the total respondents, 44.4% (100) were administrative staff, 18.7% (42) employees, 16.4% (37) professor of the subject and the rest full-time professor and academic technician.

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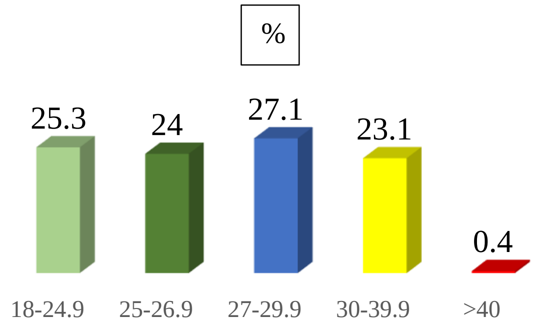


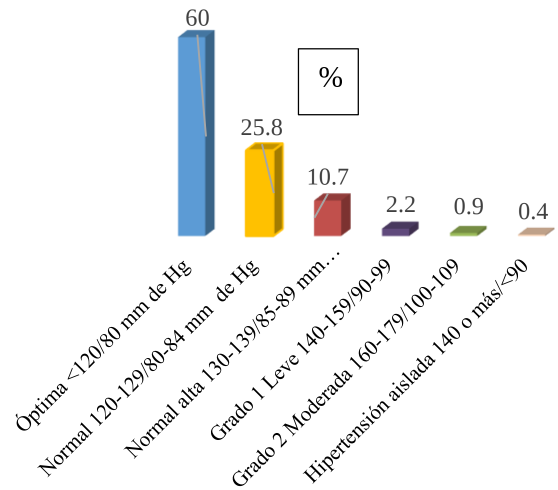
Graphic 3 Participants BMI
Source: 225 Questionnaires applied to teachers and employees

Regarding the Body Mass Index, 25.3% (57) had a normal BMI of 18 - 24.9, 27.1% (61) of 27 - 29.9, 24% (54) 25 - 26.9, and the rest lower percentages, as shown in graph 3.

Item	**Yes**		**No**	
	FREC	**%**	**FREC**	**%**
Smokes	44	19.6	181	80.4
Lives with smokers	88	39.1	137	60.9
Family history of diabetes	163	72.4	62	27.6
Family history of hypertension	153	68	72	32
Performs physical activity at least 45 minutes three times a week	70	31.1	155	68.9

Table 2 Risks related to smoking habits and hereditary family history. Morelia, Michoacán, 2017
Source: 225 Questionnaires applied to teachers and employees

Regarding smoking habits, 19.6% (44) smoke, 39.1 (88) live with smokers, thus becoming passive smokers. 72.4 (163) had a family history of diabetes mellitus, 68% (153) reported a history of hypertension. In relation to performing physical activity at least 45 minutes three times a week, 68.9% (155) does not and 31.1. (70) does.



Graphic 4 Blood Pressure of Teachers and Employees

Source: 225 Questionnaires applied to teachers and employees

85.8% had an optimal or normal blood pressure, however, 14.2% (32) presented some alteration in the figure obtained, as shown in figure 1.

Cholesterol	**Frecuency**	**%**
Less than 100	6	2.7
Normal <100	6	2.7
High 160-189	70	31.1
Very High >190	143	63.5
Total	225	100.0

Table 3 Cholesterol of teachers and employees. Morelia, Michoacán
Source: 225 Questionnaires applied to teachers and employees

The average stood at 196.8, median and mode in 200. 63.5% (143) had cholesterol> 190, 31.1% (70) 160 -189. As shown in Table 3.

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Statistical significance was found between the variables consumption of fatty meats and age with a value of r = .303 p = .000, adding salt or sugar to foods with systolic pressure, with a value of r = .230 p = .000 , as well as obesity with having a relative with hypertension with a Chi2 0.009 and RR = 2.357 (1,129 - 4,921), studies to determine cholesterol with a value of Chi2 .017 and RR = 1,613 (1,049 - 2,479). As well as the BMI with waist measurement with a value of r=.716 p=.000

Conclusion

The risks that were determined and identified in CVD in teachers and employees are hereditary family history of diabetes, arterial hypertension, Body Mass Index above normal limits, since seven out of ten of the respondents presented alteration. Although the number of smokers is not important, if we add those who live with smokers, the risk increases. Seven out of ten do not engage in physical activity. So they have four and more risk factors. It is important to implement strategies to improve behaviors related to healthy lifestyle in the study population, such as: Encourage physical activity, go to the doctor routinely to promote health and prevent diseases, healthy eating and balanced according to their needs taking into account what is established in NOM043.

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Objectives, methodology

Contribution

(150-200 words)

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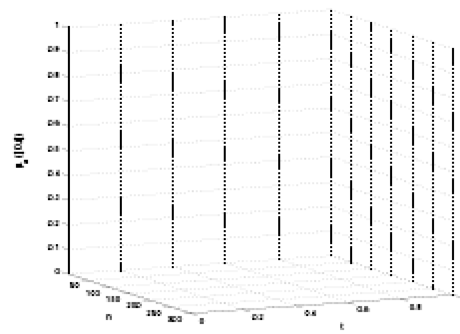

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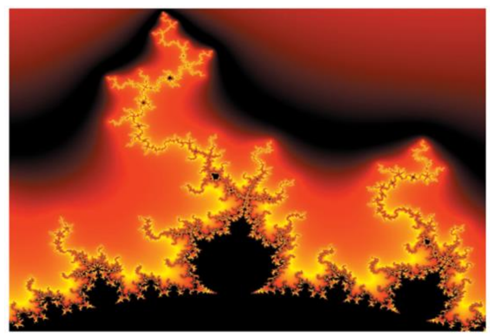

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Develop give the meaning of the variables in linear writing and important is the comparison of the used criteria.

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