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A Novel Chemical Product Design Framework with the Integration of Safety and Health Aspects

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Computer aided molecular design (CAMD) technique is a powerful tool for the design of molecules that meet a set of desirable properties. In most of the CAMD problems, the molecular physical and thermodynamic properties are often selected as the target properties while safety and health aspects have not been taken much into consideration. In this work, a novel chemical product design methodology has been developed to integrate both safety and health aspects into the CAMD framework presented by a single optimization model. The measurement of safety and health indicators are based on the molecular properties that have an impact on both of these aspects. Each property is assigned with an index or penalty value based on the degree of potential hazards. A molecule with a higher index value has a higher hazard level and vice versa. Hence, a molecule that satisfies the target properties and has a low penalty value will be selected reasonable choice. This new approach ensures that a product that possesses the desirable properties, and at the same time meets the safety and health criteria, is produced. A case study on the solvent design for gas sweetening process has been carried out to determine the optimal molecule.

1. Introduction

Many industrial disasters happened in the past point out the importance to give attention on the safety, health and environmental impact of industrial processes. This has brought about the establishment of hazard identification and analysis techniques (Palaniappan et al., 2002). These techniques are developed to control hazards in the process for minimizing the consequences of a possible accident through the installation of protective devices. However, the hazard is still present in the plant and the safety level of the plant has to rely solely on the effectiveness of the protective devices. Moreover, the installation of the add-on equipment also complicates the design and increases the capital costs (Srinivasan and Nhan, 2008). An alternate concept known as inherent safety design aims to eliminate or minimize the hazards present in the plant through the introduction of inherent safety principles into process design. However, a lot of process decisions in the plant also depend on the chemicals used for different operations. Therefore, there is a need to integrate the inherent health and safety assessment while deciding the solvents and other chemicals involved in the process.

2. Literature review

2.1 Inherent safety and health

An inherently safer process is the one that reduces the amount of hazardous chemicals and operations used in a process. An inherently safer plant is more appealing than a plant which practises conventional process concept as it has less ‘built-in’ hazard potential (Rahman et al., 2005) and less add-on protective systems which results in process simplification (Hassim and Hurme, 2010). Inherent safety has long been introduced in many applications, such as process concept evaluation, process route planning and plant

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layout design (Okoh and Haugen, 2014).The inherent safety concept should be introduced in the conceptual design stage as more engineering and financial decisions would have already been made in the later phases (Heikkilä, 1999). Probably the pioneer of all inherent safety indexes was the Prototype Index for Inherent Safety (PIIS) developed by Edwards and Lawrence (1993) to rank the inherent safety of different process. PIIS focuses mainly on the reaction step and a lower index value indicates an inherently safer route. Another index named Inherent Safety Index (ISI) by Heikkilä (1999) took into account a larger scope of process steps. These two indexes here have selected several parameters to represent the inherent safety factors, and these parameters or data are readily available during preliminary design stage. Meanwhile, the i-Safe index by Palaniappan et al. (2002) adopted some of the parameters from ISI and PIIS. For inherent occupational health, Occupational Health Hazard Index (OHHI) has been developed by Johnson (2001) for the evaluation of occupational health hazard during design phase. Process Route Healthiness Index (PRHI) by Hassim and Edwards (2006) was developed to improve the drawbacks of OHHI, but this method is still complicated as it includes a broad range of parameters to be assessed. One of the well-established inherent health indexes is the Inherent Occupation Health Index (IOHI) by Hassim and Hurme (2010) which evaluates the potential health risks of different process routes during research and development stage. Generally, the parameters that are evaluated in most of the safety and health indexes can be categorized into two aspects. The chemical-related parameters are usually assessed by the physical and chemical properties of the molecule. The process-related parameters evaluate the inherent safety and the potential of exposure for the process itself.

2.2 Computer-aided molecular design (CAMD)

CAMD is a reverse problem of property prediction method where the identity of the molecule must be identified based on the given set of molecule building blocks and a particular set of target properties. The principal objective of CAMD is to determine a compound that exhibits the specified properties. In order to generate a chemically feasible molecular structure, CAMD employs a set of molecular fragments or building blocks and to estimate the specified properties of the molecular structure. These properties can be estimated by using group contribution methods (GCM), where the contributions for a specific property of each fragment or group present in the compound are summed up to calculate the compound property value. A set of feasible molecules are generated which satisfy those property specifications (Achenie et al., 2003). Recently, CAMD techniques have been applied to design the optimal ionic liquid for carbon dioxide capture (Chong et al., 2014). In most CAMD problems, the target properties are usually represented in terms of physical and thermodynamic properties of the molecule. The safety and health aspects are usually not taken into account during the design stage as both aspects are only evaluated during performance analysis phase to select molecules that are safer and healthier to human.

3. Modelling methodology

The main objective of this work is to establish a systematic framework that applies both CAMD and inherent safety and health indexes simultaneously, in order to generate inherently safer and healthier molecules that meet the desired target properties. This proposed design includes problem formulation, inherent safety and health indexes selection, model development, and molecular design.

3.1 Problem formulation

This stage begins with the identification of the needs of a chemical product by defining the product specifications to determine the functionality and behaviour of a product. These product specifications can be translated in terms of target properties. These target properties are usually represented by the physical and thermodynamic properties of the molecules. The desired properties will then be selected as the design objectives that the generated molecules need to achieve in order to serve its function.

3.2 Inherent safety and health indexes selection

The selection of the inherent safety and health indexes are based on the existing indexes that have already been well developed. For safety indexes, PIIS, ISI and i-Safe are considered. These indexes are developed for process route selection in which several safety-related parameters are evaluated to represent the inherent safety factors. The parameters that are related to the chemical properties are heat of reaction, heat of side reaction, chemical interaction, reactivity, flammability, explosiveness, toxicity and corrosiveness. In a CAMD problem, it is easier to apply the parameters that can be directly linked to the properties which can be estimated through property prediction models. Parameters in which the index scores are assigned based on non-numerical descriptions may not be easily included in the mathematical optimization model. For instance, the corrosiveness subindex from ISI is based on the basis of the required construction material, such as carbon steel, stainless steel and special materials. This categorization of corrosiveness cannot be represented in terms of mathematical model. Therefore, two

parameters are chosen from the safety indexes, namely flammability (I_{FL}) and explosiveness (I_{EX}). These parameters can be represented in terms of flash point, boiling point (flammability) and explosion limits (explosiveness). Toxicity exposure is not chosen to avoid the repetition of this parameter as it has already been included in one of the health indexes (Hassim and Hurme, 2010). The index scores for explosiveness subindex are taken from ISI while the score for flammability subindex is taken from NFPA flammability rating (National Fire Protection Association, 2007). Even though PIIS also offers explosiveness index scores, the maximum score assigned is ten, which is relatively high compared to the maximum index score given by ISI and NFPA. For consistency purpose, explosiveness index scores from ISI are applied. On the other hand, the reason for applying the NFPA flammability rating is that it is one of the standard systems that is commonly applied to classify the hazards of the materials, as it is frequently used in the material safety data sheet (MSDS).

As for health indexes, the two indexes studied are PRHI and IOHI. Only the chemical-properties parameters will be chosen to represent the inherent health index, which include viscosity (I_η) from PRHI, material phase (I_{MS}), volatility (I_V) and exposure limit (I_{EL}) from IOHI. Another parameter named acute health hazard (I_{AH}) will also be included in which the scoring for this subindex will be based on the NFPA health hazard rating (National Fire Protection Association, 2007). From the NFPA health hazards, the potential of a material to cause injury due to contact with or entry into the body via inhalation, skin contact, eye contact, or ingestion is addressed. These can be measured using LC_{50} for acute inhalation toxicity, LD_{50} for acute dermal toxicity, and LD_{50} for acute oral toxicity. Since the group contribution model for LD_{50} (acute oral toxicity) is available, it will be applied in this subindex. The total penalty score of a molecule (I_{SHI}) is the summation of all the subindex scores assigned to it, which is shown in Eq(1). A molecule with lower total penalty score is desired as it indicates an inherently safer and healthier molecule.

$$I_{SHI} = I_{FL} + I_{EX} + I_{\eta} + I_{MS} + I_{V} + I_{EL} + I_{AH} \quad (1)$$

3.3 Model development

In this stage, all the properties that are considered in the design objectives and the inherent safety and health indexes parameters have to be calculated through the property prediction models. One of the most notable approaches used is GCM, which is able to estimate the physical and chemical properties of a molecule based on its molecular structure. The property can be determined by summing the frequency of each group occurring in the molecule multiplied by its contribution (Marrero and Gani, 2001). Permissible exposure limit (PEL) and LD_{50} for acute oral toxicity can be estimated using GCM models developed by Hukkerikar et al. (2012a). Physical properties like flash point (F_p), normal boiling point (T_b) and melting point (T_m) are estimated using GCM models developed by Hukkerikar et al. (2012b). Conte et al. (2008) have established a GCM model to calculate viscosity (η). Both upper explosion limit (UEL) and lower explosion limit (LEL) can be estimated using correlations developed by Ma et al. (2013).

After a molecule that meets the design objectives is generated, the index score will be assigned to the molecule depending on its property. For instance, for the viscosity subindex (I_η), if the viscosity of the molecule falls in between 0.1 cP and 1 cP, a scoring of one will be assigned. If the viscosity falls between 1 cP and 10 cP, then a scoring of two will be assigned and so on. These viscosity intervals here have created a disjunction for the constraint. To solve this issue in the optimization model, disjunctive function can be applied to describe abrupt changes over a certain decision variable. The method used to model the disjunctive function can be referred to El-Halwagi (2012).

3.4 Molecular design

In this final stage, the developed optimization model is employed to identify the optimum molecule that fulfils the design objectives or target properties. Firstly, the possible molecular group acting as the potential building blocks are selected. Next, the structural constraints and target property range are specified and implemented to eliminate combination of infeasible solution. In order to ensure that a molecule is generated, structural feasibility constraints has been included in the problem formulation.

4. Case study: solvent design for gas sweetening process

4.1 Optimization formulation

The objective of this case study is to determine a solvent that will replace methyl diethanolamine (MDEA) as the absorbent which can help in minimizing the usage of amine solution in the acid gas removal unit. At the same time, the aspects and safety and health will also be taken into consideration during the molecular design phase. The target properties chosen for this case study include heat of vaporization (H_v), vapour pressure (VP), molar volume (V_m), molecular weight (M_w), viscosity (η), normal boiling point (T_b) and

melting point (T_m). The molecule should have minimum soil sorption coefficient (log K_{oc}) to prevent the accumulation of the escaping solvent in one place (Chemmangattuvalappil and Eden, 2013) and minimum total penalty score (I_{SHI}) for an inherently safer and healthier molecule. The property targets at standard condition (298 K and 1 atm) for this case study are listed in Table 1.

Table 1: Property targets for molecular design

Property	Lower bound	Upper bound	Property	Lower bound	Upper bound
H_v (kJ/mol)	50	528	*VP* (mm Hg)	-	11
V_m (cm^3/mol)	40	224	M_w (g/mol)	60	250
η (cP)	-	460	T_b (°C)	111	350
T_m (°C)	-65	25			

The molecular blocks selected are based on the conventional absorbents that are utilised in gas sweetening process. The selected molecular blocks include CH_3, CH_2, CH, OH, CH_2O, CH_2NH_2, CH_2NH, CHNH, CH_3N and CH_2N. GCM models developed by Hukkerikar et al. (2012b) can be used to estimate H_v and V_m. *VP* cannot be predicted by GCM, but it can be calculated from T_b using an empirical relationship (Sinha and Achenie, 2003). Meanwhile, log K_{oc} can be calculated through a correlation (Seth et al, 1999) given in terms of octanol-water partition coefficient (log K_{ow}). log K_{ow} can be calculated using GCM by Hukkerikar et al. (2012b). The property operators are formed with respect to the target properties and the lower and upper bounds are calculated as shown in Table 2.

Table 2: Property operators and targets

Property *j*	Ω_j	LB	UB	Property *j*	Ω_j	LB	UB
H_v	$H_v - H_{v0}$	40.3873	518.3873	*VP*	$\exp(T_b/T_{b0})$	5.2289	-
V_m	$V_m - V_{m0}$	0.024	0.208	M_w	M_w	60	250
η	$\ln \eta$	-	6.1312	T_b	$\exp(T_b/T_{b0})$	4.8117	12.7879
T_m	$\exp(T_m/T_{m0})$	4.2623	7.9779	log K_{oc}	log K_{ow} - K_{ow}	-2.6284	3.7313
I_{SHI}	I_{SHI}	10	13				

4.2 Fuzzy optimization

By using the lower and upper bounds of H_v, *VP*, V_m, M_w, η, T_b and T_m as constraints, the lower and upper bounds of log K_{oc} and I_{SHI} are determined via optimization approach. However, the molecule which performs better may not necessarily exhibit a low penalty score. Hence, a decision making has to be made on the trade-off between the target performance of the molecule and its inherent safety and health level. This results in a multi-objective optimization problem and fuzzy optimization algorithm is thus applied to ensure that both desirable product functionality and the safety and health criteria have been attained. Both criteria to be optimized are represented by the linear membership functions as shown in Eq(2) and (3):

$$\frac{3.7313 - \Omega_{\log K_{oc}}}{3.7313 + 2.6284} \geq \lambda \tag{2}$$

$$\frac{13 - \Omega_{I_{SHI}}}{13 - 10} \geq \lambda \tag{3}$$

where λ is a continuous variable representing the degree of satisfaction, which ranges from 0 to 1. In order for both $\Omega_{\log Koc}$ and Ω_{ISHI} to approach their respective lower limit, the value of λ has to be close to 1. Hence, the objective function of this case study is to maximize the value of λ. The optimization model is a mixed integer nonlinear programming (MINLP) as it involves one nonlinear constraint due to the formulation of acute health hazard subindex. Therefore the global optimum solution cannot be guaranteed. Integer cut constraints are applied to enumerate alternative solutions to enhance the confidence level of the solutions.

5. Results and discussion

From optimization results, the best five molecules with the highest λ value are shown in Table 3 and 4.

Table 3: The best five solvents and their properties

Solvent	Chemical structure	λ	log K_{oc}	I_{SHI}	H_v (kJ/mol)	VP (mm Hg)	V_m (cm^3/mol)
A1	$CH_3CH(OH)N(CH_3)CHOCH_3$	0.670	-0.654	10	65.59	2.617	125.9
A2	$CH(OH)_2N(CH_3)_2$	0.667	-1.863	11	78.89	1.627	83.4
A3	$CH_3CH_2N(CH_2OH)_2$	0.667	-1.656	11	77.15	0.618	100.6
A4	$CH_3CH_2NHO(CH_2)_2OH$	0.667	-1.523	11	61.31	2.457	109.8
A5	$CH_3CH_2CH(OH)CH_2NH_2$	0.667	-1.512	11	62.18	2.787	97.7

Table 4: The best five solvents and their properties (continued)

Solvent	M_w (g/mol)	η (cP)	T_b (°C)	T_m (°C)	F_p (°C)	UEL-LEL (vol%)	PEL (ppm)	LD_{50} (mg/kg)
A1	119.164	7.79	163.15	-15.42	96.84	8.93	1.03	533.93
A2	91.110	43.51	173.33	22.78	120.77	14.04	2.24	749.01
A3	105.137	31.38	193.59	18.23	97.39	10.92	2.99	800.27
A4	105.137	8.63	164.52	7.68	80.88	10.92	1.10	644.52
A5	89.138	8.15	161.79	13.85	67.32	10.16	8.15	869.24

Table 5: The best five solvents and their subindex scores

Solvent	I_{FL}	I_{EX}	I_η	I_{MS}	I_V	I_{EL}	I_{AH}
A1	1	1	2	2	0	3	1
A2	1	1	3	2	0	3	1
A3	1	1	3	2	0	3	1
A4	2	1	2	2	0	3	1
A5	2	1	2	2	0	3	1

From Table 3, it is showed that solvent A1 has the highest λ value. Even though A1 does not have the lowest log K_{oc} value, its total penalty score (I_{SHI}) is the lowest among all five solvents. The solvents with the next highest λ value are A2, A3, A4 and A5. Since these four solvents have the same I_{SHI} value, they are ranked according to their log K_{oc} value. Table 5 shows a breakdown of seven subindex scores allocated to each solvent. One of the major drawbacks of these safety and health indexes is that the subindex scores are assigned to the molecule through discrete value. This causes the integration of safety and health aspects on the molecule to be less sensitive as the property value that falls within the same interval will be assigned a similar subindex score. For instance, molecules with *PEL* value within 1 to 10 ppm are assigned a subindex score of 3 while molecules with *PEL* value within 10 to 100 ppm are assigned a score of 2. Now consider that molecule *P* has a *PEL* of 3 ppm while molecule *Q* has a *PEL* of 8 ppm. Both molecules receive a similar subindex score of 3, even though molecule *Q* has a higher *PEL* value, which indicates that it is inherently healthier than molecule *P*. Another issue is the abrupt change of the subindex score when the property value moves across the boundary of the range. Now consider another molecule *R* with *PEL* of 11 ppm, even though it has a *PEL* value difference of 3 ppm compared to molecule *Q*, it receives a score of 2. Meanwhile, molecule *P* and *Q* have a higher *PEL* value difference, but they both received the same score. Hence, one way to solve these issues is to modify the subindex to ensure a continuous change in the scoring. In this way, the scoring becomes more sensitive as the final penalty score (I_{SHI}) for each generated molecule may no longer be similar. Besides, some of the parameters from the safety and health indexes that are not included in this work may be formulated into the optimization model in the future given more detailed research are done on these. This can definitely enhance the final index scoring as a wider scope of safety and health aspects can be covered.

6. Conclusions

A single-stage chemical product design framework employing CAMD methods has been developed to design a molecule with low safety and health hazards level that also meets a set of desired properties. The safety and health parameters from the existing safety and health indexes that are relevant to the chemicals are used to evaluate the safety and health aspects of the molecules. Disjunctive optimization algorithm is applied for assigning the subindex scores to the molecule based on its property value. A case study on the solvent design for a gas sweetening process is carried out and fuzzy optimization is applied to develop molecules that simultaneously achieve high functionality and high safety and health performance. Some of

the issues encountered when applying the index score is discussed. Future work can be conducted to improve the sensitivity of the index scoring and to cover a broader range of safety and health parameters.

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