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Abstract

Purpose: Cardiovasc is the patented product name of Amlodipine besylate. Its intended design is aimed for vasodilatory action primarily used in treating stable and variant angina, and hypertension. This study aims to validate the linearity of absorbance of the reference standard with Cardiovasc drug concentration. Moreover, the drug concentration elucidation from the samples aims to quantitate the correlation of the marketed patented drug for commercial use as possible source of environmental pollutants known as greenhouse gases.

Methodology: Ultraviolet-visible spectroscopy is used to measure the absorbance of the drug samples, Amlodipine besylate reference standard and Cardiovasc, for validation of linearity with drug concentration using the electron excitement from HOMO to LUMO of anti-bonding energy levels for catalytic analysis of drug concentration. Interaction with uncertainties, risks, and capabilities is a tool for decision making of health effects and economic impacts to sustainable development.

Findings: The results from Ultraviolet-visible spectroscopy shows that minimal drug concentration exposed as discharge to the environment will not exhibit any linear correlation as significant contributor of environmental pollutants. The commercial drug, Cardiovasc, follows the second range of Amlodipine besylate reference standard, hence, Cardiovasc effluents play a critical role to the quality design of marketed drug in terms of medical research methods as this procedure is done as exclusion to the acquired drug patentability intended to exercise their healthcare corporate governance as fulfillment of monetary goals in business ethics of sustainable development.

Recommendations: This legal validation highlights the significance of linear correlation of patented drug to environmental effects as social responsibility of corporate healthcare governance. Hence, the International Trade Law enables the marketed drug product to perform its intended action as well as to advocate sustainable development goals as "commercial" in nature. As the European Patent Commission clearly states that medical research methods are excluded from the patentability coverage of drug product, this paper strongly recommends innovation of tools, engineering on eradicating greenhouse gases as sources of environmental pollutants that play a crucial factor to climate change.

Keywords: *Catalysis, Environmental Governance, Healthcare Waste, Greenhouse Gases, Economic Impact*

INTRODUCTION

Amlodipine besylate falls under the dihydropyridine type of calcium channel blocker which has a slow onset of vasodilatory action. Its primary use is for the treatment of variant and stable angina, and to lower blood pressure in hypertension. This drug is presumed to be a reducing agent due to the presence of amino group on its chemical structure. Thus, applications of inorganic oxidants into the drug will reduce divalent elements to their lower level, and together with the ligand, will exhibit their respective colors under exclusion in medical research methods.[1]

World Health Organization (WHO) defined healthcare waste (HCW) as a characterized wasted produced from medical centers, hospitals, healthcare facilities, and research establishments intended for immunization, diagnosis, treatment, and related research. WHO has enumerated and specified HCW into ten categories, where each type is defined and documented in several papers. The major sites of HCW are medical clinics, hospitals, healthcare camps, dispensaries, medical and biomedical laboratories, mortuary and autopsy centers, medical research centers, animal research and hospitals, and blood banks. The results of poor healthcare waste management (HCWM) are adverse effects in public health and environment. The most commonly cited problems in suitable HCWM are usually safe waste disposals, occupational health and safety for healthcare staffs and unlawful scavenging. Safe HCW disposal entails four key stages such as segregation, collection and storage, treatment, transport and safe disposal where national legislative rules and policies must be complied. Four major types of HCW suggested for an organized segregation and storage isolation, disposal and collection are: infectious and non-infectious sharps, infectious non-sharp wastes, general wastes, and hazardous wastes. Collection, storage, and remediation of these wastes vary from one another. Many countries had already adopted incineration, disinfection, sterilization, plasma arc, and land filling as HCW treatment. Majority of developing Asian countries employs incineration in their infectious sharps and pathological wastes with rare application of needed air pollution as control and the ash is disposed together with the municipal waste. Chemical liquid wastes are known to be collected and remediated via hospital discharge treatment system, and disposed into municipal effluents. However, treatment efficacy is uncertain. Pharmaceutical wastes, such as expired medicines, are usually in lack of attention for appropriate disposal.[2]

An increasing number of hospitals and other medical facilities are gaining attention of the demand to facilitate waste pharmaceuticals produced in healing patients and develop programs in their practices for answering the problems. In comparison, some discarded medicines are subject to hazardous waste management and disposal standards. The awareness was brought by others through detection in waterways, such as surface waters, wastewater, groundwater and, to a lesser extent, drinking water, at nanogram to low micrograms per liter.[3]

The number of cancers is progressing constantly worldwide resulting to a reasonable treatment consumption augmentation. These treatments are radiotherapy and chemotherapy which can be utilized in combination or not. Chemotherapy is known by action mechanism of anticancer drugs

[1] Nafisur Rahman, Manisha Singh, and Nasrul Hoda, 'Application of oxidants to the spectrophotometric determination of amlodipine besylate in pharmaceutical formulations' (2004) 59(11) *Il Farmaco* 913.
[2] A. Prem Ananth, V. Prashantini, and C. Visvanathan, 'Healthcare waste management in Asia' (2010) 30 *Waste Management* 154.
[3] Bill Brewer and Andrea Antell, 'A case study of the management of hazardous waste drugs in a large university hospital, (2013) 20(3) *Journal of Chemical Health and Safety of the American Chemical Society* 2.

having toxic attributes for cells, and of which most are categorized into three types by the International Agency for Research on Cancer (IARC): carcinogenic impact for humans (class 1); likely carcinogenic (class 2); and potentially carcinogenic (class 2B). Cytostatic drugs react through inhibition of cell growth or directly killing of cells in an unselective means targeting both tumoral and healthy cells. Hence, several antineoplastic agents have fighting effects on cytotoxicity, mutagenicity, carcinogenicity, embryotoxicity and teratogenicity. During the recuperation period, these drugs are observed via urinal and fecal elimination of patients in large proportion under metabolite forms or parent compounds. Hospital discharges, which are commonly emitted directly to the effluent network in lack of pretreatment, represent an "undebatable" emission source of several bioactive compounds utilized for research and medical purposes such as radioisotopes, pharmaceuticals, or solvents. Although several of these substances are eliminated through biodegradation or adsorption in wastewater treatment plants, some molecules are directly emitted into the environment where they appear to be a potential toxic hazard in public health and ecosystems via drinking water.[4]

Between 1999 and 2000, he US Geological Survey evaluated 139 streams across 30 states to ascertain the presence of 96 drug hormones, pharmaceuticals, and other organic wastewater contaminants (OWCs). 13% of the streams sampled contained more than 20 OWCs, and 82/95 OCWs were sourced in at least one stream. Additional reports have discussed that the main sources of pharmaceuticals passing the surface water are treated and untreated municipal wastewater effluents emitting into surface waters and inappropriate disposal of discarded medicines by customers and medical facilities. US studies have shown that a several pharmaceuticals are detected at low levels in finished drinking water in concentrations of approximately 40 ng/l. In Europe, studies are evident that pharmaceuticals in tap water appear in concentrations from a few nanograms to low micrograms per liter. The US Environmental Protection Agency published a 2009 report as an emerging concerns on the detection of particular contaminants, which comprises of various pharmaceuticals traced in 9 wastewater treatment sewage system. Pharmaceuticals including sulfamethoxazole, doxycycline, naproxen, and erythromycin were found in one or more of the sewage systems tested.[5]

Comparing wastewater emitted by households, recent investigations have documented significant concentrations of X-ray contrast media, disinfectants, pharmaceutical compounds, and resistant microbiological loads in hospital effluents. Spanish surface waters revealed a high drug component concentrations in a study, as found in rivers usually located in downstream, particularly, of a hospital, pharmaceutical plant, university campus, and a large retirement home. The samples had a total drug compound concentration of 78.7 μg/l, and with a single contribution of the antiepileptic drug carbamazepine of 67.7 μg/l.[6]

[4] N. Mater, F. Geret, L. Castillo, V. Faucet-Marquis, C. Albasi, and A. Pfohl-Leszkowicz, '*In vitro* tests aiding ecological risk assessment of ciprofloxacin, tamoxifen and cyclophosphamide in range of concentrations released in hospital wastewater and surface water, (2014) 63 *Environment International* 191.

[5] Bill Brewer and Andrea Antell, 'A case study of the management of hazardous waste drugs in a large university hospital, (2013) 20(3) *Journal of Chemical Health and Safety of the American Chemical Society* 2.

[6] Raphael Janssens, Mrinal Kanti Mandal, Kashyap Kumar Dubey, and Patricia Luis, 'Slurry photocatalytic membrane reactor technology for removal of pharmaceutical compounds from wastewater: Towards cytostatic drug elimination, (2017) 599-600 *Science of the Total Environment* 613.

This study seeks to determine if Amlodipine besylate has a reducing capacity on metal compound (i.e. to convert Fe^{+3} to Fe^{+2}) with an aid of a ligand to form complexation reaction. Furthermore, it aims to quantitate the amount of light absorbed by the sample using Ultraviolet-visible spectrometer from a known concentration range of amlodipine besylate for detection of drug amount present in each concentration as the light passes through the sample. Thus, it intends to compare the quality of the sample commercial product with the reference standard. Moreover, the absorbance of the drug samples is designed to elucidate its detrimental effects of expired medicines to the environment as molecular flux of greenhouse gases characterized by wavelengths of Ultraviolet-visible spectroscopic measurements under the principle of environmental catalysis.

MATERIALS AND METHODS

Preparation of Reagents

Preparation of a Reference Standard Solution

An amount equivalent to 0.1055 g of Amlodipine besylate reference standard was weighed using an analytical balance and dissolved to minimum volume of glacial acetic acid diluted to 100 ml distilled water using a volumetric flask to make a 0.1% Amlodipine besylate stock solution.[7]

Preparation of 0.25% Ferric Ammonium Sulphate Solution

A stock solution was prepared by mixing 0.43 ml of concentrated H_2SO_4 with 99.57 ml of distilled water to make a 0.08 M sulfuric acid. Subsequently, 0.25 g of ferric ammonium sulfate was weighed and dissolved to 100 ml of 0.08 M H_2SO_4 to make a 0.25% ferric ammonium sulfate solution and was transferred to 250-ml Duran bottle.

Preparation of 0.6% 1,10 – Phenanthroline Solution

0.6 g of 1,10 – phenanthroline was weighed and dissolved to 100 ml of ethanol to make a 0.6% 1, 10 – phenanthroline solution and was transferred to a 250-ml Duran bottle.

Preparation of Sodium Acetate-Acetic acid buffer solution

6.805 g of sodium acetate was dissolved in 250 ml distilled water to make a 0.2 M sodium acetate. 3.0025 g equivalent to 2.86 ml of acetic acid was mixed with 250 ml distilled water to make a 0.2 M acetic acid. The prepared 0.2 M sodium acetate was mixed with 0.2 M acetic acid to make a 500 ml sodium acetate-acetic acid buffer solution and its pH was adjusted to 4.6 using a pH meter.[8]

Validation Procedure

Method A

Aliquots corresponding to 2 µg/ml, 4 µg/ml, 6 µg/ml, 8 µg/ml and 10 µg/ml, or a range of 2-10 µg/ml, of amlodipine besylate standard solution were pipetted into a series of tubes labeled as Std-1, Std-2, Std-3, Std-4, and Std-5. Table below served as reference as to how many µl. will be taken from the reference standard to follow the range and how many milliliters of prepared reagents will be added to the test tubes:

[7] Nafisur Rahman, Manisha Singh, and Nasrul Hoda, 'Application of oxidants to the spectrophotometric determination of amlodipine besylate in pharmaceutical formulations' (2004) 59(11) *Il Farmaco* 914.
[8] Nafisur Rahman, Manisha Singh, and Nasrul Hoda, 'Application of oxidants to the spectrophotometric determination of amlodipine besylate in pharmaceutical formulations' (2004) 59(11) *Il Farmaco* 915.

Table 1: Amlodipine Besylate Standard Solution

Standard	Volume	0.25% Fe $NH_4(SO4)_2$	$NaCH_3COO$-CH_3COOH Buffer Solution	0.6% 1, 10 – Phenanthroline Solution
1	50 µl	5.0 ml	6.25 ml	1.25 ml
2	100 µl	5.0 ml	6.25 ml	1.25 ml
3	150 µl	5.0 ml	6.25 ml	1.25 ml
4	200 µl	5.0 ml	6.25 ml	1.25 ml
5	250 µl	5.0 ml	6.25 ml	1.25 ml
Blank 0	---	5.0 ml	6.25 ml	1.25 ml

After the addition of reagents to the different sets of reference standard, the 6 test tubes were placed on a water bath for 30 min to develop the color. After heating, the test tubes were cooled to room temperature and were transferred to a 25 ml volumetric flask and completed up to mark by distilled water. The absorbances were recorded against their respective reagent blanks prepared at 500 nm using Ultraviolet-visible spectrometer.[9]

[9] Nafisur Rahman, Manisha Singh, and Nasrul Hoda, 'Application of oxidants to the spectrophotometric determination of amlodipine besylate in pharmaceutical formulations' (2004) 59(11) *Il Farmaco* 915.

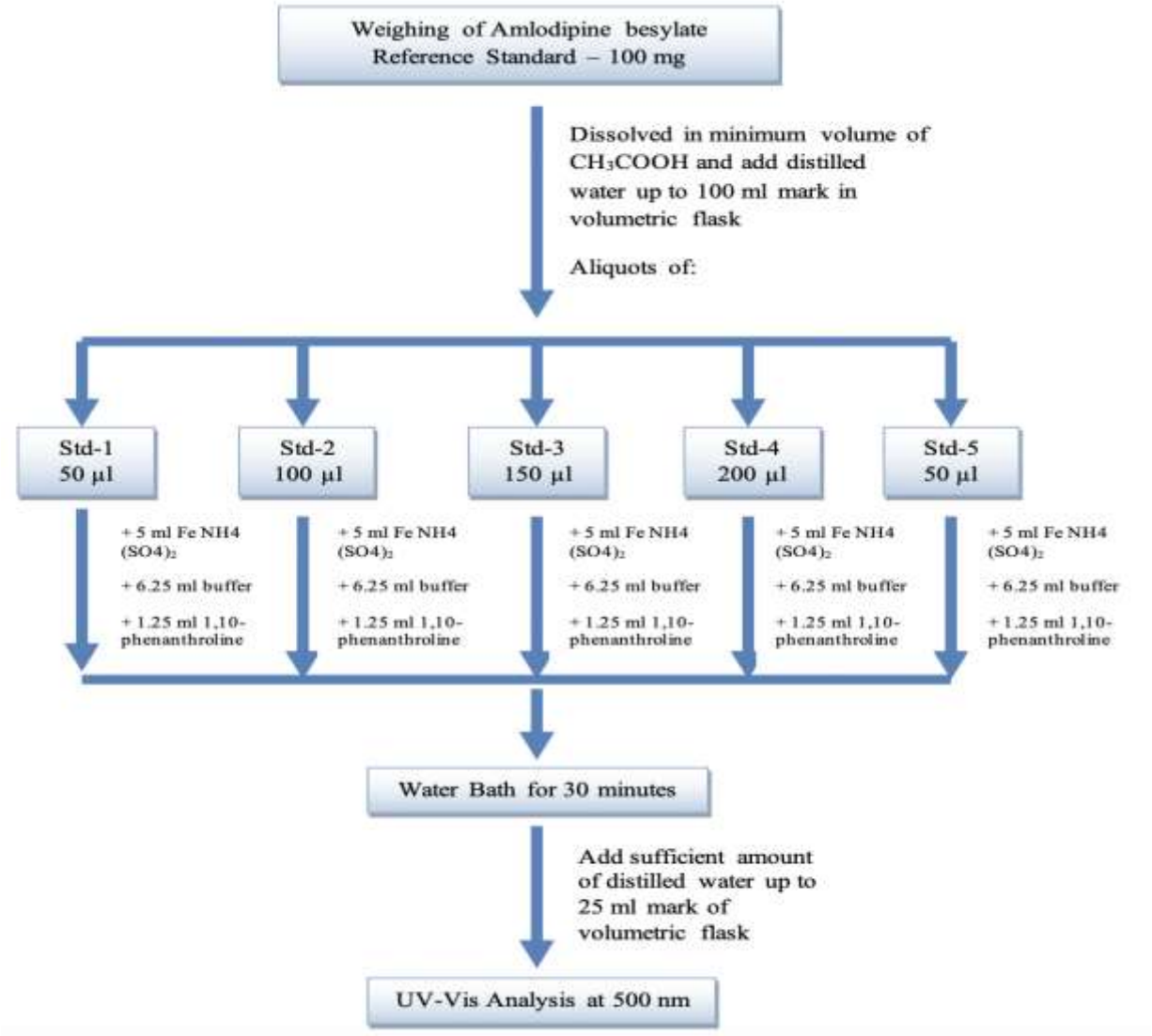

Figure 1: Schematic Diagram of Reference Standard to UV-Vis Analysis

Commercial Product Analysis

Ten tablets of Cardiovasc were purchased from a local drugstore. Total weight was quantified, and the average weight was calculated. It was grinded and powdered using mortar and pestle. The contents were transferred into a vortex tube and extracted by adding sufficient volume of chloroform. Extraction was done by shaking the tube using a vortex mixer for 5 minutes. The content was filtered and evaporated to dryness. Dry residue was dissolved with 10 ml glacial acetic acid and diluted with distilled water and made up to mark using a 50 ml volumetric flask. Assay of commercial product was done following the aliquots made in methods 2, 3 and 4 of reference standard. Schematic diagram is shown below.[10]

[10] Nafisur Rahman, Manisha Singh, and Nasrul Hoda, 'Application of oxidants to the spectrophotometric determination of amlodipine besylate in pharmaceutical formulations' (2004) 59(11) *Il Farmaco* 916.

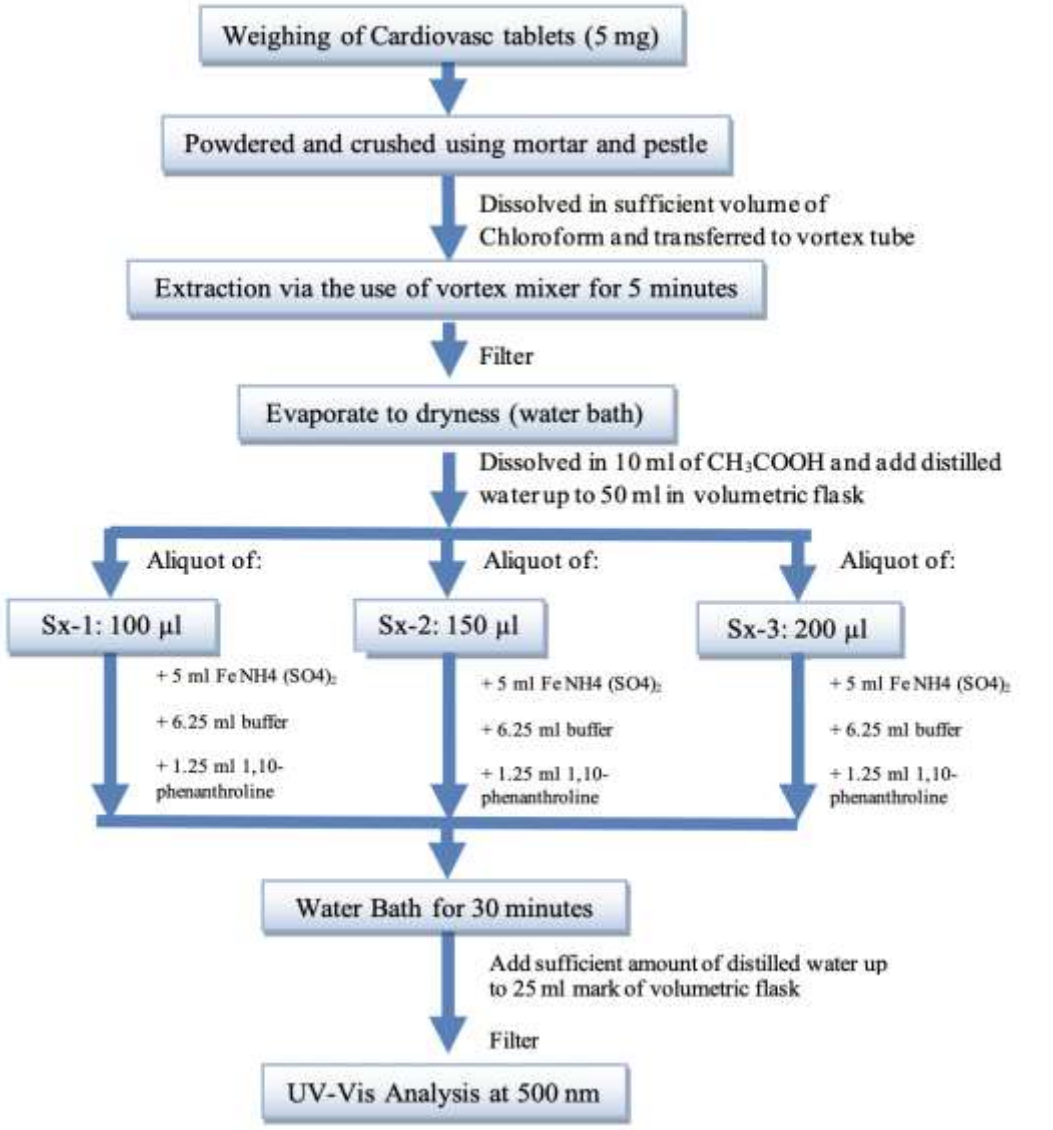

Figure 2: Schematic Diagram of Cardiovasc to UV-Vis Analysis

Risk-Based Decision Making

Pharmaceutical and fine chemical industries withstand significant problems in product and process development due to uncertainties and risks related with market competition, strict regulatory requirements, product failure, escalating development expenditures and long development time. Several strategies are utilized to avoid or lessen uncertainties and risks related with these elements. It is worthwhile to assess the whole development life cycle instead of a particular development stage due to the similarities in associations and interactions between various product stages and process life cycles. Thus, recent literature has increasingly gained attention on process systems approach to interpret the action of these complex chemical development architectures. Early chemical development plays a crucial role in controlling subsequent life cycle stages. It starts by assessing the potential synthetic routes in the presence of competing sustainable development

goals such as safety, health, environment, and economics factors. Ideally, any experienced researcher can synthesize a given molecule in various ways through multi-stage syntheses, using distinct raw materials, catalysts, solvents, reagents, and intermediates. However, many of these multi-stage syntheses options, commonly known as synthetic route options, are related with several uncertainties at the early development stages due to insufficient knowledge associated to business, legal, technical, and social landscapes in which products are to be manufactured and consumed. Hence, successful synthesis lies not only on the intrinsic attributes of the molecule made, such as active ingredient, but also on how the molecular development is planned and implemented, and on the effective management of important resources such as time, effort, and costs. Therefore, there is a vast pressure for teams of process development to make appropriate decisions at the right time due to its impact on the transcription of the product and process life cycles aiming satisfaction on the need for a cheaper and timely work.[11]

In the first step, uncertainty of each route is quantified and represented by an uncertainty result. In lack of historical data, qualitative models are employed to determine the uncertainty degree. These qualitative prototypes could be expressed as word models to amount the ambiguity of uncertainty. Uncertainty assessment is finally evident as uncertainty result to compare and further measure the risk of distinct route options. In the second step, risk evaluation is performed based on availability of data. The raised classic duplet-questions, 'what is the frequency of the uncertain element to occur?' and 'what are the outcomes?', are investigated to assess the likelihood and consequences. But the results are represented in terms of probabilities. The risk is then explained by multiplying the frequency and impact to assess the severity degree. Finally, risk assessment is shown as risk quantified in comparing and ranking various route options. In the third step, capability assessment is done to evaluate the effort needed to lessen the uncertainty. This comprises the resources, both human and facilities, how much time and cost are consumed in performing these experiments, analyses, and modelling. This is to diminish the uncertainties involved in each area of a specified route option as precursory to these analyses. The capability analysis is then represented as capability measured result in comparison of various route options. The actions done in each route option is plotted against the three quantified results of uncertainty, risks and capability for further decision-making. This application supports the decision maker to compare various options targeting fulfillment of sustainable development goals rather than intuitive perception resulting to "gut feeling" judgement. [12]

[11] A. Manipura, E.B. Martin, G.A. Montague, P.N. Sharratt, and I. Houson, 'Risk-based decision making in early chemical process development of pharmaceutical and fine chemical industries, (2013) 55 *Computers and Chemical Engineering* 71.

[12] A. Manipura, E.B. Martin, G.A. Montague, P.N. Sharratt, and I. Houson, 'Risk-based decision making in early chemical process development of pharmaceutical and fine chemical industries, (2013) 55 *Computers and Chemical Engineering* 72.

DISCUSSION

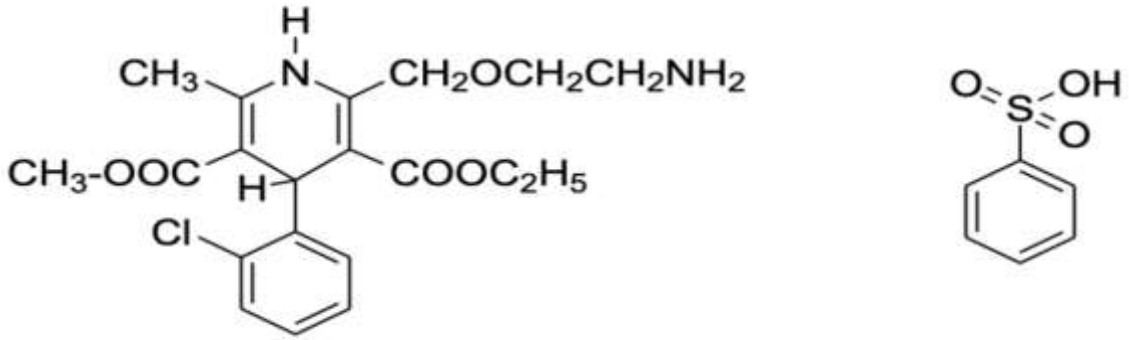

Figure 3: The Chemical Structure of Amlodipine Besylate

The Amlodipine besylate structure is shown in Figure 3. The presence of the amino group is an indicator of the reducing capacity of the drug. In this study, the ferric (Fe^{+3}) metal present in Fe NH_4 $(SO_4)_2$ was reduced to ferrous (Fe^{+2}) and reacted with the ligand, 1, 10 –phenanthroline to form red colored complexes, in which pH was maintained through the presence of a buffer. The equations below, rationalizes the chemical reaction occurred in method A:

$$\} \text{---}CH_2OCH_2CH_2NH_2 + 2\ Fe\ NH_4\ (SO4)_2 \rightarrow \} \text{---}CH_2OCH_2CH_2N^{+}\text{-}Fe^{-}SO_4 + Fe\ (NH4)_2\ (SO4)_2 + H_2SO_4$$

Amlodipine Besylate — Ferric Ammonium Sulfate

$$\text{ortho-Phenanthroline} + Fe^{+2}\text{-Amlodipine besylate} \rightarrow \text{O.P.T.-A.B.} + Fe^{+2}$$

(Red color formation)

The commercial product of Amlodipine besylate, Cardiovasc, after extracting the active ingredient, also developed a red color formation after the addition of reagents noted on the previous page and followed the chemical equations above. Both the reference standard and the market drug, which are called generically amlodipine besylate, were subjected for Ultraviolet-visible analysis, in which same functional group will be analyzed for its ability to shift its ground state (Highest Occupied Molecular Orbital) to an excited state (Least Unoccupied Molecular Orbital) known as HOMO→LUMO via the radiation coming from the visible region. In this case, the lone pair of electrons, η, and the bonding molecular orbital, π, all from the amino group, will be excited, thus exhibiting symbols, σ*, for the anti-bonding lone pair and π*, for the anti-bonding orbital, due to the absorption of different amounts of energy. Hence, the general pattern of energy levels and molecular transitions are illustrated in Figure 4:[13]

[13] Robert Silverstein, G. Clayton Bassler, and Terence Morrill, *Spectrometric Identification of Organic Compounds* (John Wiley & Sons, 1974) 235.

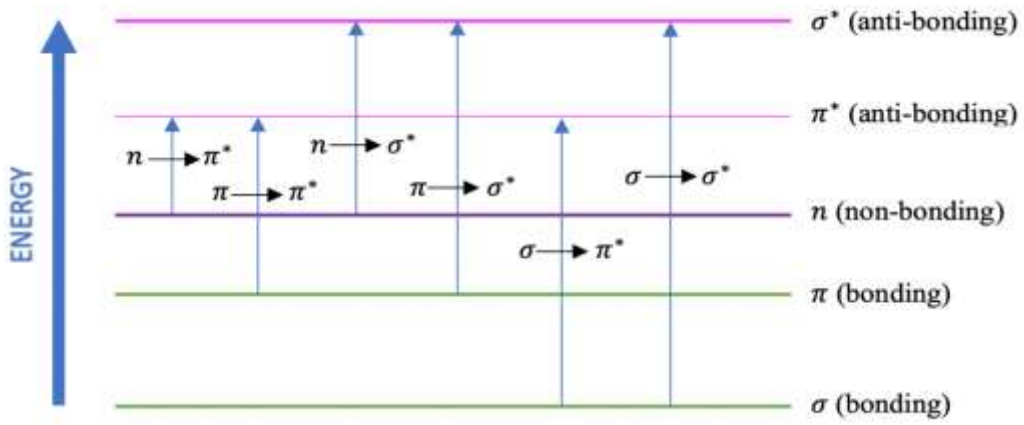

Figure 4: Summary of Electronic Energy Levels

Thus, the absorption of energy set at a definite wavelength, 500 nm, spawns absorbance readings. The data shown below are measurements for the spectrophotometric determination of Amlodipine besylate, both in reference standard (see Table 2) and market drug (see Table 3).

Table 2: Absorbance of Amlodipine Besylate Reference Standard

Sample ID	Type	Conc.	WL 500.0	Wt. Factor
1	Std.	2	2.269	1
2	Std.	4	2.282	1
3	Std.	6	2.280	1
4	Std.	8	2.280	1
5	Std.	10	2.288	1

Table 3: Absorbance of Cardiovasc (Amlodipine Besylate)

Sample ID	Type	Conc.	WL 500.0
1	Unknown	6.810	2.281
2	Unknown	14.141	2.294
3	Unknown	12.565	2.291

The concentration range of amlodipine besylate reference standard was in its simplest form, starting from 2 µg/ml, up to 10 µg/ml. In other words, from the starting material of 105.5 mg amlodipine besylate reference standard dissolved in minimum volume of glacial acetic acid and diluted up to 100 ml volumetric flask, making a concentration of 0.1055 g/100 ml, or 1055 µg/ml in reduced form. Pipetting the respective volume in the reference standard stock solution will make the distinction in every aliquot based on its increasing concentration. Figure 5 represents the plotting of the concentration range of reference standard against their absorbance value.

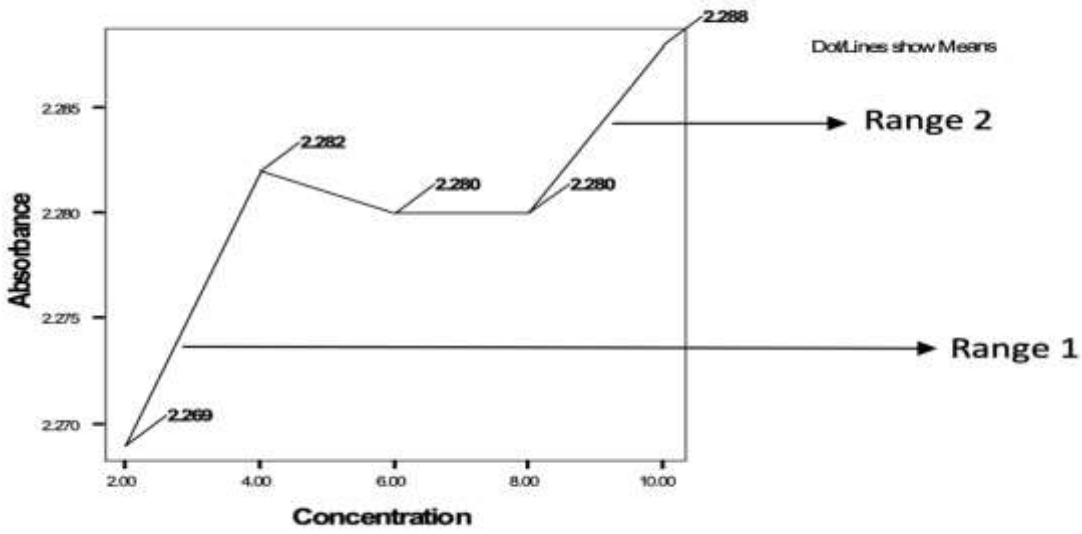

Figure 5: Absorbance Values of Reference Standard

The graph above (see Figure 5) has shown a broken linearity which is indicative that the subject of study has two ranges instead of one. These ranges would indicate that there are two separate clusters of scope in obtaining accuracy and precision and thus, the increasing concentration is not proportional. This was supported by linear regression analysis that did not obtain a value very close to 1, that the slope plotted was non-linear.

On the other hand, Cardiovasc, the marketed product of Amlodipine besylate, had a linear slope. This would indicate that its linear regression computation has a value of 1 or very close to 1. The observed plot is shown in Figure 6.

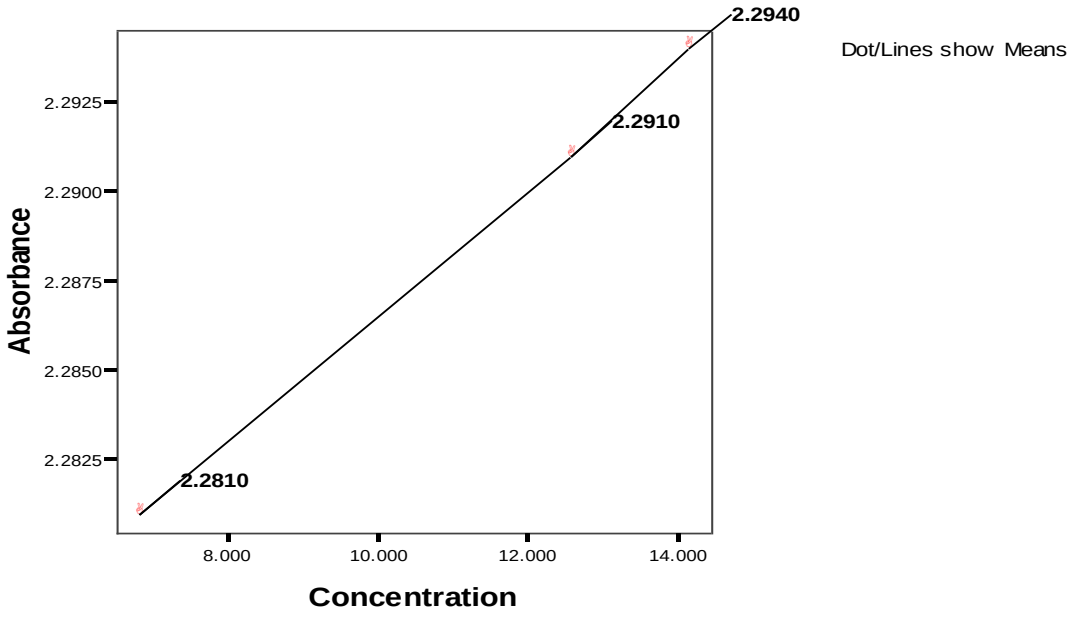

Figure 6: Absorbance Values of Cardiovasc

Regression Analysis

Table 4: Amlodipine Besylate Reference Standard

	X value	Y value	XY value	X^2 value	Y^2 value
	2	2.269	4.538	4	5.148
	4	2.282	9.128	16	5.208
	6	2.280	13.680	36	5.198
	8	2.280	18.240	64	5.198
	10	2.288	22.880	100	5.235
TOTAL	30	11.399 ~ 11	68.466 ~ 68	220	25.987 ~ 26

$$r = \frac{\{n\Sigma XY - (\Sigma X)(\Sigma Y)\}}{\sqrt{n\Sigma X^2 - (\Sigma X)^2}\sqrt{n\Sigma Y^2 - (\Sigma Y)^2}} \quad (1)$$

$$r = \frac{\{(5)(68) - (30)(11)\}}{\sqrt{(5)(220)} - (30)^2\sqrt{(5)(26)} - (11)^2} \quad (2)$$

$$r = 0.238 \quad (3)$$

$$r^2 = 0.06 \quad (4)$$

A correlation coefficient of 0.238 indicates a poor linear relationship between concentration and absorbance. Since $r^2 = 0.06$, it shows that only 6% of the variation in the absorbance values is

accounted for by a linear relationship with concentration. Hence, this supports the non-linearity of the graph of the reference standard for amlodipine besylate.

Table 5: Cardiovasc (Amlodipine Besylate)

	X value	Y value	XY value	X^2 value	Y^2 value
	6.810	2.281	15.53361	46.3761	5.203
	14.141	2.294	32.439454	199.967881	5.262
	12.565	2.291	28.786415	157.879225	5.249
TOTAL	33.516 ~ 34	6.866 ~ 7	76.75949 ~ 77	404.223206 ~ 404	15.714 ~ 16

$$r = \frac{\{n\Sigma XY - (\Sigma X)(\Sigma Y)\}}{\sqrt{n\Sigma X^2 - (\Sigma X)^2}\sqrt{n\Sigma Y^2 - (\Sigma Y)^2}} \quad (5)$$

$$r = \frac{\{(3)(77) - (34)(7)\}}{\sqrt{(3)(404)} - (34)^2\sqrt{(3)(16)} - (7)^2} \quad (6)$$

$$r = 0.9358 \quad (7)$$

$$r^2 = 0.90 \quad (8)$$

The correlation coefficient of Cardiovasc has a very good linear relationship, obtaining a value of 0.9358. Its coefficient of determination, r^2, expresses a proportion of 0.9, in which 90% of the total variation of the absorbance values of the sample obtains a linear slope relationship with concentration values. Hence, a linear correlation is observed for the quantitative analysis of the commercial drug product.

Equations

Integral and differential methods of deriving rate expressions from varying change in concentration (ΔC) and absorbance (ΔAbs) per unit of time ascertains the enthalpy change from energy binding capacity to anti-bonding energy levels based on Gibbs free energy following zero-order rate of catalytic reaction. Rate constants are necessary in order to observe the constant ratios between reaction rates and reactant concentrations and can be expressed as Michaelis-Menten constant, molar absorptivity and activation energy. These expression constants describe the time functions starting from the initial concentration at t=0 or path at b=0 cm until the desired time with corresponding change in concentration. The derivation of change in concentration and absorbance in respect with time or path is shown in the general equation: y = mx + b. Derivation of molecular flux equations for greenhouse gas emissions is illustrated in Equations (1) to (56).[14]

a. Adsorption Kinetics

$$[Fe - PW] = \frac{[Fe_T][PW_i]}{K_m + [PW_i]} = \frac{[PW_{max}][PW_i]}{K_m + [PW_i]} = \frac{[dPW_f][PW_i]}{K_m + [PW_i]} \quad (9)$$

[14] James Welty, Charles Wicks, Robert Wilson, and Gregory Rorrer, *Fundamentals of Momentum, Heat, and Mass Transfer* (John & Wiley Sons, Inc, 2007).

$$\frac{[Fe_T]}{[Fe-PW]} = \frac{[PW_{max}]}{[Fe-PW]} = \frac{[\Delta PW]}{[Fe-PW]} = \frac{K_2+K_3}{K_1} = K_m \quad (10)$$

b. Desorption Kinetics

$$[Fe-PW] = \frac{[dPW_f][PW_i]}{K_m+[PW_i]} \quad (11)$$

$$\frac{[\Delta PW]}{[Fe-PW]} = K_m \quad (12)$$

c. Partition Coefficient

$$K_{MD} = \frac{W}{V} x \frac{\Sigma_{i=1}^{n} Q^0_{water,i}/\left(1+\left(W/VK_{SD_i}\right)\right)}{\Sigma_{i=1}^{n} Q^0_{water,i} - \Sigma_{i=1}^{n} Q^0_{water,i}/\left(1+\left(W/VK_{SD_i}\right)\right)} \quad (13)$$

$$\log K_{owmix} = \log[\sum x_i (K_{ow})_i] \quad (14)$$

where:

K_{MD} = C18 Empore disk/water partition coefficient for a mixture

W = volume of the solution

V = volume of the hydrophobic phase

$Q^0_{water,i}$ = initial amount of chemical *i* in water

K_{SD_i} = partition coefficient of a single chemical

$$D_{MPW} = \frac{W}{V} x \frac{\Sigma_{i=1}^{n} Q^0_{water,i}/\left(1+\left(W/V\varepsilon_{SPW_i}\right)\right)}{\Sigma_{i=1}^{n} Q^0_{water,i} - \Sigma_{i=1}^{n} Q^0_{water,i}/\left(1+\left(W/V\varepsilon_{SPW_i}\right)\right)} \quad (15)$$

d. Hooke's Law

$$\bar{\nu} = \frac{1}{2\pi c}\sqrt{\frac{f}{(M_x M_y)/(M_x+M_y)}} \quad (16)$$

where:

$\bar{\nu}$ = the vibrational frequency (cm^{-1})

c = velocity of light (cm/s)

f = force constant of bond (dyne/cm)

M_x *and* M_y = mass (g) of atom *x* and atom *y*, respectively

e. Beer's Law

$$A = \log\left(\frac{I_0}{I}\right) = \varepsilon bc \quad (17)$$

where:

I_0 = incident light intensity

I = intensity of transmitted light

ε = molar absorptivity (or molar extinction coefficient)

b = cell path length in cm

c = sample concentration (moles/L)

$$A = \log\left(\frac{I_0}{I}\right) = \varepsilon bc \quad (18)$$

$$\frac{\Delta I}{db} = \varepsilon c \quad (19)$$

$$\frac{\Delta I}{c} = \varepsilon db \quad (20)$$

$$[Abs]_T = \varepsilon b + [Abs]_0 \quad (21)$$

$$y = mx + b \quad (22)$$

f. Enthalpy Change/EA/Gibb's Energy (Adsorption)

$$\ln[C]_T = \left(-\frac{E_a}{R}\right)\left(\frac{1}{T}\right) + \ln[C]_0 \quad (23)$$

$$y = mx + b \quad (24)$$

g. Rate Law (Zero Order Kinetics)

$$[A]_T = -kt + [A]_0 \quad (25)$$

$$y = mx + b \quad (26)$$

h. Convective Mass Transfer between Phases

h.1 Distribution Law Coefficient (Partition of a solute between 2 immiscible liquids)

$$C_{A,liquid\ 1} = KC_{A,liquid\ 2} \quad (27)$$

where:

C_A = concentration of solute A in the specified liquid phase

K = partition or distribution coefficient

h.2 Henry's Law Constant (Equilibrium relation for gas and liquid phases where dilute solutions are involved)

$$p_A = Hc_A \quad (28)$$

where:

p_A = equilibrium partial pressure of component A in the vapor phase above the liquid phase

H = Henry's law constant

c_A = equilibrium composition of A in the dilute liquid phase

h.3 Raoult's Law (Liquid Phase is Ideal)

$$p_A = x_A P_A \quad (29)$$

where:

x_A = mole fraction of A in the liquid phase

P_A = vapor pressure of pure A at the equilibrium temperature

h.4 Dalton's Law (Gas Phase is Ideal)

$$p_A = y_A P \quad (30)$$

where:

y_A = mole fraction of A in the gas phase

P = total pressure of the system

h.5 Raoult-Dalton Equilibrium Law (2 Phases are Ideal)

$$y_A P = x_A P_A \quad (31)$$

h.6 Liquid Phase – Rate Equations

$$N_A = k_L \Delta c_A \quad (32)$$

where:

$$k_L = \frac{moles\ of\ A\ transferred}{(time)(area)(mol/volume)} \quad (33)$$

$$N_A = k_x \Delta x_A \quad (34)$$

where:

$$k_x = \frac{moles\ of\ A\ transferred}{(time)(area)(mole\ fraction)} \quad (35)$$

h.7 Gas Phase – Rate Equations

$$N_A = k_G \Delta p_A \quad (36)$$

where:

$$k_G = \frac{moles\ of\ A\ transferred}{(time)(area)(pressure)} \quad (37)$$

$$N_A = k_c \Delta c_A \quad (38)$$

where:

$$k_c = \frac{moles\ of\ A\ transferred}{(time)(area)(mol/volume)} \quad (39)$$

$$N_A = k_y \Delta y_A \quad (40)$$

where:

$$k_c = \frac{moles\ of\ A\ transferred}{(time)(area)(mole\ fraction)} \quad (41)$$

h.8 Unsteady-state Mass Flux Between 2 Phases

$$N_{A,z} = k_G(p_{A,G} - p_{A,i}) = -k_L(c_{A,L} - c_{A,i}) \quad (42)$$

$$-\frac{k_L}{k_G} = \frac{(p_{A,G} - p_{A,i})}{(c_{A,L} - c_{A,i})} \quad (43)$$

h.9 Unsteady-State Molecular Diffusion

$$\frac{\partial c_A}{\partial t} = D_{AB} \frac{\partial^2 c_A}{\partial z^2} \quad (44)$$

with Initial and Boundary Conditions:

$$c_A = c_{A0} \qquad at\ t = 0 \qquad for\ 0 \le z \le L$$

$$c_A = c_{As} \qquad at\ z = 0 \qquad for\ t > 0$$

$$c_A = c_{A\infty} \qquad at\ z = \infty \qquad for\ t > 0$$

Dimensionless Concentration Change (Y)

$$Y = \frac{C_{A\infty} - C_{As}}{C_{As} - C_{A0}} \quad (45)$$

$$\frac{\partial Y}{\partial t} = D_{AB} \frac{\partial^2 Y}{\partial z^2} \quad (46)$$

with Initial and Boundary Conditions:

$$Y = Y_0 \qquad at\ t = 0 \qquad for\ 0 \le z \le L$$

$$Y = 0 \qquad at\ z = 0 \qquad for\ t > 0$$

$$Y = 0 \qquad at\ z = \infty \qquad for\ t > 0$$

Product Solution to the PDE

$$Y(z,t) = T(t)Z(z) \quad (47)$$

PDE's:

$$\frac{\partial Y}{\partial t} = Z \frac{\partial T}{\partial t} \quad (48)$$

$$\frac{\partial^2 Y}{\partial z^2} = T \frac{\partial^2 Z}{\partial z^2} \quad (49)$$

$$Z \frac{\partial T}{\partial t} = D_{AB} T \frac{\partial^2 Z}{\partial z^2} \quad (50)$$

h.10 Flux at any position z

$$N_{Az} = -D_{AB}\frac{\partial C_A}{\partial z} \quad (51)$$

h.11 Flux using Rate Equations

$$N_A = -k_L\frac{\partial^2 c_A}{\partial z^2} \quad (52)$$

$$N_A = k_G\frac{\partial^2 c_A}{\partial z^2} \quad (53)$$

with Initial and Boundary Conditions:

$$c_A = c_{A0} \qquad at\ t = 0 \qquad for\ 0 \le z \le L$$

$$c_A = c_{As} \qquad at\ z = 0 \qquad for\ t > 0$$

$$c_A = c_{A\infty} \qquad at\ z = \infty \qquad for\ t > 0$$

Dimensionless Concentration Change (Y)

$$Y = \frac{C_{A\infty} - C_{As}}{C_{As} - C_{A0}} \quad (54)$$

$$N_A = -k_L\frac{\partial^2 Y_A}{\partial z^2} \qquad N_A = \left[-k_{L,t}\frac{\partial\left(\frac{C_{A\infty}-C_{As}}{C_{As}-C_{A0}}\right)}{\partial t}\right] + \left[\left(-k_{L,z}\right)\frac{\partial\left(\frac{C_{A\infty}-C_{As}}{C_{As}-C_{A0}}\right)}{\partial z}\right] \quad (55)$$

$$N_A = k_G\frac{\partial^2 Y_A}{\partial z^2} \qquad N_A = \left[k_{G,t}\frac{\partial\left(\frac{C_{A\infty}-C_{As}}{C_{As}-C_{A0}}\right)}{\partial t}\right] + \left[\left(k_{G,z}\right)\frac{\partial\left(\frac{C_{A\infty}-C_{As}}{C_{As}-C_{A0}}\right)}{\partial z}\right] \quad (56)$$

with Initial and Boundary Conditions:

$$Y = Y_0 \qquad at\ t = 0 \qquad for\ 0 \le z \le L$$

$$Y = 0 \qquad at\ z = 0 \qquad for\ t > 0$$

$$Y = 0 \qquad at\ z = \infty \qquad for\ t > 0$$

Decision Making Framework

The life cycle of drugs starting from research synthesis up to waste disposal via pyrolysis created emissions of greenhouse gases (CO_2, CH_4 and NOx), and thermal energy that contribute to climate change that may increase detrimental environmental impacts leading to global warming and human diseases such as cardiovascular disease, chronic obstructive pulmonary disease, asthma and malaria in future estimates. Factors causing environmental risks from pharmaceutical drug sector such as greenhouse gases and thermal energy generate risk outcomes of environmental and health dangers (see Figure 7) are necessary to evaluate extensively the likelihood and seriousness of the issues involved.[15]

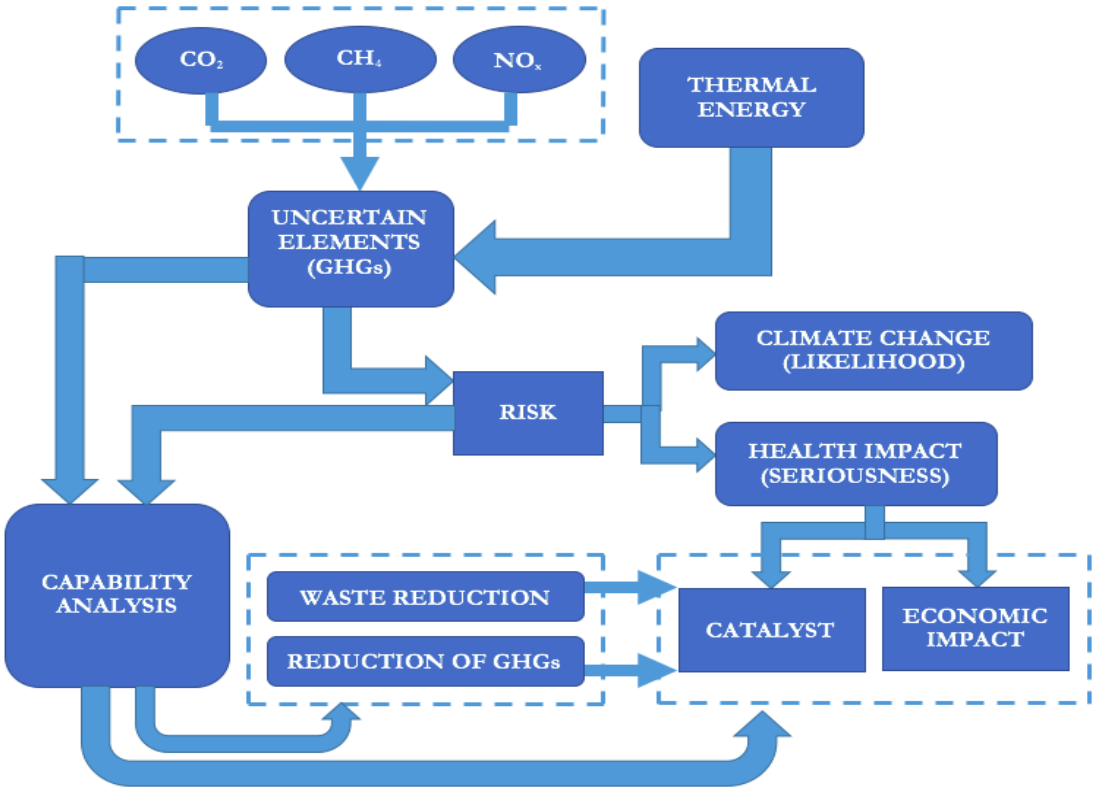

Figure 7: Interaction between Uncertainty, Risk and Capability

The United Nations Convention on Contracts for the International Sale of Goods (CISG) has resolved dissimilarities observed in culture, language, and legal operation for the global provision of widely recognizing contract process in relation to selling of goods. This convention highly augments the potential ability of international trade to expand the interpretation and application of contract law in harmony with its ultimate design as efficiency must be directly associated with the sale of goods.

[15] Zharama Llarena, 'Targeting Factors of Ecotax Based on Cradle-to-Grave of Carbon Footprint for SELECT Criteria Mechanism of Decision Process Using Waste-to-Energy Technology, (2022) 11(1) *American Journal of Energy Engineering* 11.

In 1981, the Working Group created and drafted model law for International Contract Practices. Subsequently, after a 21-day diplomatic conference on 1985, United Nations Commission on International Trade Law (UNCITRAL) adopted a new model law system designed to be applied limitedly to arbitrations concerning international commercial transactions. Thus, there is a strong demand to employ commercial laws to its utmost extent beyond a particular territory. It is apparent that commercial laws vary technically per jurisdiction, thus, legal principles must be exercised to apply those mechanisms to disputed limitations since the practice of law should be made comparable to other regions. Based on Article 1(3), international arbitration is considered in the specified matter of conditions, such as business places of parties involved, and their contract performance are not within the same jurisdiction or country. Meanwhile, Article 1(1) defines on its explanatory footnote that "commercial" in nature must be broadly interpreted to cover all aspects of transactions to emphasize the fulfillment of economic goals in relation to business ethics.

The European Patent Convention (EPC) emphasized the value of innovative research to pharmaceutical firms. Unfortunately, policy justifications removed patent protection involving mitigations based on medical research methods. Based on article 53(c) EPC 20002, its exclusion pertains to therapeutic and surgical methods of human and animal treatment, as well as its diagnostic practices. Hence, the products used for medical treatment are not considered as exclusions to remove their patent protection, as specified in their official declaration of therapeutic compositions. Hence, these substances used to heal people has restrained its patent rights over medical treatment justified policy exclusions, in such a way that refusing to acknowledge its second-use patents would result in innovation denial against its appropriate reward. Moreover, United Kingdom, Netherlands, and Denmark expressed paragraph 2(d) replacement at Article 50 with Article 52, under paragraph 5, stating that no provisions must be deemed as removing patent protection, consisting of its declared therapeutic substance intended as a treatment design away from making policies on medical, surgical, and diagnostic practices. Hence, United Kingdom clearly draws a line between product patentability and second-use design.[16]

CONCLUSION

Cardiovasc is a registered drug product of Amlodipine besylate designed for vasodilatory mechanism of action. Under medical research methods using Ultraviolet-visible spectroscopy, Amlodipine besylate has been successful in reducing the Ferric (Fe^{+3}) metal in Fe NH_4 $(SO_4)_2$ into its lowest level, Ferrous (Fe^{+2}), with the help of a ligand, 1, 10 – Phenanthroline, to visibly observe the change of color into red hue formation. The commercial product, Cardiovasc, has almost the same amount of drug compared to the reference standard, under Range 2, relative to its absorbance readings which are based on the amount of visible light absorbed per drug concentration. In other words, an increase in the amount of concentration will also have an increment on the amount of light absorbed due to the presence of ground state electrons of the amino group which can be excited upon the passing of light, hence, the concentration of drug is directly proportional to the amount of light. Thus, the commercial product chosen is of good quality since the amount of active ingredient is quantitatively almost the same with reference standard. However, Range 1 absorbance is the ideal drug concentration to prevent correlation of drug discharge as possible

[16] Zharama Llarena, 'UNCITRAL Model Law Development of Arbitration Framework for EPC Disclosure of Travaux Preparatoires Using Political Expedience of Tax Planning, (2022) 5(4) *International Journal of Law and Society* 380.

source of greenhouse gases. The analytical procedure using Ultraviolet-visible spectroscopy serves as the validation instrument to elucidate and correlate environmental catalysis of drug action as simulation to the body during its shelf-life and interactions to the environment when disposed as expired medicine. Furthermore, the decision-making process based on uncertainties, risks, and capabilities serves as exclusion to Patent Law for fulfillment of sustainable development goals comparable to other territories practicing Trade Law as "commercial" in nature. Corporate governance is a systematic design of stakeholders and their corporate social responsibility to advocate sustainable development. Drug wastes are social responsibility under healthcare corporate governance. This paper highlights that linearity of correlation of drug products for commercial use, under Patent Law intended to treat people with ailments, must undergo corporate social responsibility of sustainable development. Thus, International Trade Law dictates it to exercise the marketing of their products and services as also "commercial" forces of nature as human recuperation under drug treatment must be observed in a natural way of recovery with significant correlation to environmental public health and its ecosystem. Therefore, this study highly recommends to innovate appropriate tools suitable in engineering treatments to environmental pollution in advocacy to fight climate change.

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