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Fate of Zidovudine through Water Treatment with Chlorine: A Kinetic Study

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Abstract

Advances in water quality Analysis indicate that antibiotics are rising pollutants owing in the direction of their unbroken contribution in addition to determination in the aquatic ecosystem still at small concentrations. Researchers across the world reveal that in environmental matrices, indicating conventional treatment methods are inefficient in their removal. To put off this pollution; numerous processes to degrade/ eliminate antibiotics have been calculated. Present report lecture to the current state of knowledge relating to the degradation and elimination processes applied to a specific class of antibiotics. Several inorganic and organic micro pollutants can go through reactions with chlorine. Chlorine reactivity is inadequate in the direction of exacting sites (mainly amines, reduced sulfur moieties) and is frequently pragmatic during chlorination processes. HOCl is the chief hasty chlorine species during chlorination processes. To better know /predict chlorine reaction in the company of micro pollutants, the kinetics and mechanistic in sequence on chlorine reactivity, this Research was taken up. The present study reveals that degradation levels are highest at low pH ranges and able to remove about 50% under standard test conditions.

Keywords: Chlorination, degradation, kinetics, pharmaceutical drug, spectrophotometer, Zidovudine etc.

Introduction

Zidovudine (ZDV) is a Nucleoside Analog Reverse Transcriptase Inhibitor (NRTI). Zidovudine is a kind of antiretroviral drug[1,2]. Zidovudine is man-made drug in the company of pyrimidine nucleoside analogue energetic adjacent to HIV-1, AIDS and pre- AIDS. Zidovudine has a molecular formula of $C_{10}H_{13}N_5O_4$ and molecular weight of 267.24 g/mol. The structural formula is shown in figure -1. Zidovudine is a white to light brown, fragrance-free, crystalline solid in addition to it is easily soluble in ethanol (95%), watchfully soluble within water. The drug is authoritatively planned in United States of Pharmacopiea[3]. Numerous systematic techniques with the purpose of have been reported on behalf of the evaluation of Zidovudine in organic liquid or pharmaceutical formulations consist of UV-Visible Spectrophotometer and High Performance Liquid Chromatography.

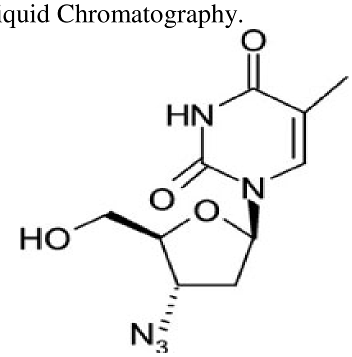

Figure-1
Structure of Zidovudine

Several consumption water sources have been polluted with pesticides, pharmaceuticals and anti microbial agents, in addition to other potentially harmful chemicals. The destiny for several of these compounds beneath drinking water treatment conditions is of major alarm due to their potential unfavorable health effects excite distribution of antibacterial among inhabitant bacteria. A huge portion of the total clinically given antibacterial load is discharged into municipal waste water systems, which symbolize a main path for way in of such human use antibacterial agents into natural aquatic environment[4].

Chlorination is a chemical process frequently used in water treatment mainly for dis-infection. Consumption water disinfection usually involve the utilize of chlorine by the side of one or two points in the treatment process, i.e., for pretreatment and/or for post-treatment. Due to their capability for disinfection (microorganisms) and oxidation, substance oxidants are universally worn in water treatment processes[5].

Pharmaceuticals together with antibiotics' are nearby within municipal sewage, chiefly like a effect of human excretion. Numerous lively antibiotics aren't entirely metabolized throughout healing use and hence go in sewage through excretion in an unaffected type. The planned discarding of unexploited drugs hooked on the sewer as well as veterinary use in addition adds to the quantity of antibiotic originates inside sewage. Waste from veterinary clinics and runoff from agricultural applications into municipal sewers are besides probable sources of veterinary antibiotics in wastewater. The reported levels of exact antibiotic drugs detected in raw sewage come into view to change among countries, maybe shimmering changeable recommendation practices in addition to difference within per capita water use foremost to a variety of degrees of strength[6].

Material and Methods

All hard work was made to completion the conduction of experiments with standard procedures as per standard literature referred.

A stock solution of zidovudine was arranged via dissolving suitable sum of sample within distilled water. A stock solution of HOCl was set by taking an suitable volume of 5% NaOCl in deionised water[4]. The stock solution was then uniformed by iodometry and DPD (N, N-Diethyl-P-Phenylenediamine)-FAS (Ferrous Ammonium Sulfate) titrimetry respectively. 0.02M acetate buffer {pH= 4 to pH= 5}, phosphate buffer {pH=6 to pH=8.5}, in addition to borate buffer {pH =9} were used to uphold invariable pH through experiment conducted in reagent water[7].

All reagents were of analytical grade: i. The Rate of Degradation was assessed i.e (Kinetic Rates) by; CARY 50 Bio UV-Vis Spectrophotometer, ii. Varian BV, The Netherlands) with temperature controller was instrumental. iii. For pH analysis, an Elico pH meter model LI 120 was used.

Kinetic Measurements: The kinetic measurement was performed under pseudo first order condition by means of HOCl was as a minimum ten fold molar excess over ZDV at an invariable Ionic strength using 0.02 mol dm^{-3} buffers. The reaction was initiated via assimilation thermostatted solutions of HOCl in addition to ZDV which in addition contains essential volume of buffers. The temperature was consistently maintained at (25 ± 0.2)°C. The reason of the effect was followed via monitoring lessen in absorbance of ZDV as role of time in 1 centimeter path length quartz cell of Carry 50 Bio UV-Visible spectrophotometer. The purpose of Beer's law of ZDV at λ_{max} 266 nm had been confirmed philanthropic $\varepsilon = 10116\ dm^3\ mol^{-1}\ cm^{-1}$ Pseudo first order rate constant, k'obs was evaluated beginning the plots of log $(A_t - A_\infty)$ against time, where 'A' refers in the direction of absorbance at any time t and t_∞ is at never-ending time which exclude the absorbance of several products of ZDV throughout the reaction[7]. The first-order plots in approximately all the case was linear up to 80% conclusion of the reaction and k´obs table-1.

Assortment of Analytical Concentration Ranges: Commencing standard stock solution of Zidovudine, suitable of a portion of a total amount of a solution were pipetted out into 10 mL volumetric flasks and dilutions were prepared in the company of distilled water on the way to find operational standard solutions of concentrations from 2 to 50 µg / mL. Absorbances in favor of these solutions were measured by the side of 266 nm. The most of numerous pharmaceuticals compounds present in the range of microgram per liter in water so in order to decide the concentration the ranges are fixed in analytical range. The concentrations of the standards must lie within the working range of the technique (instrumentation)[8].

Table-1
Effect of variation of [HOCl] and [ZDV] on the rate of chlorination of ZDV at 25⁰C. Ionic strength; 0.02 mol dm^{-3} at 25⁰C

pH	[HOCl](M)	[ZDV](M)	k obs(s^{-1})
3	$3.22x10^{-4}$	$5x10^{-5}$	$3.0x10^{-3}$
	$6.45x10^{-4}$	$5x10^{-5}$	$3.10x10^{-3}$
	$9.67x10^{-4}$	$5x10^{-5}$	$5.0x10^{-3}$
	$1.29x10^{-3}$	$5x10^{-5}$	$5.78x10^{-3}$
	$1.92x10^{-3}$	$5x10^{-5}$	$6.50x10^{-3}$
	$3.22x10^{-4}$	$1x10^{-5}$	$1.47x10^{-3}$
	$3.22x10^{-4}$	$2x10^{-5}$	$1.56x10^{-3}$
	$3.22x10^{-4}$	$3x10^{-5}$	$1.63x10^{-3}$
	$3.22x10^{-4}$	$4x10^{-5}$	$1.63x10^{-3}$
	$3.22x10^{-4}$	$5x10^{-5}$	$1.50x10^{-3}$

Calibration sweep for the Zidovudine: Correct volumes of a portion of a total amount of a solution as of standard Zidovudine stock solution was taken to dissimilar volumetric flasks of 10 mL capability. The quantity was used to the mark in the company of distilled water to achieve concentrations of 1, 2, 3,4,5,6 and 7 µg / mL. Absorbance are shown in table-2 and spectrum of respective solution against distilled water as blank were measured at 266 nm in addition to the graphs of absorbance alongside concentration was plotted and shown in figure-2. Optical characteristics of Zidovudine are shown in table-3.

Table-2
Results of calibration curve at 266nm for Zidovudine by Visible Spectroscopy

Sl.no	Concentration(µg/ml)	Absorbance at 266nm
1	1	0.146
2	2	0.264
3	4	0.482
4	5	0.499
5	6	0.653
6	7	0.865

Table-3
Optical Characteristics of Zidovudine

Parameters	Results
Absorption maximum	266 nm
Beer's law limit (µg / ml)	2-20 µg / ml
Correlation coefficient (r^2)	0.997
Regression equation (y = mx + c)	Y = 10116x + 0.057

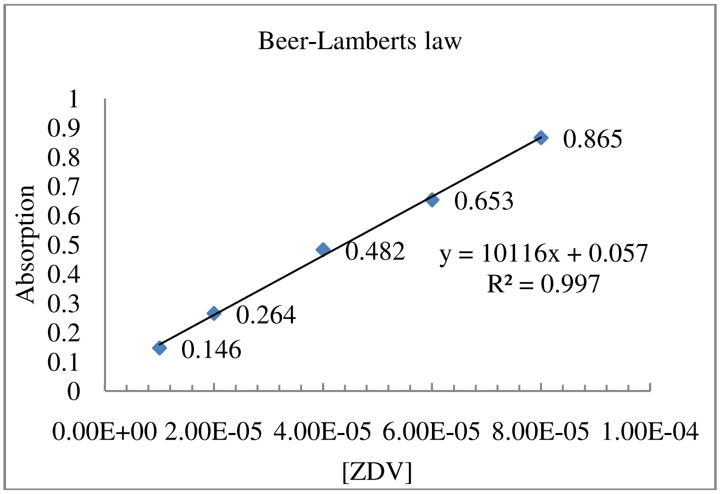

Figure-2
Linearity plot or calibration cures for Zidovudine at 266 nm by Visible Spectroscopy

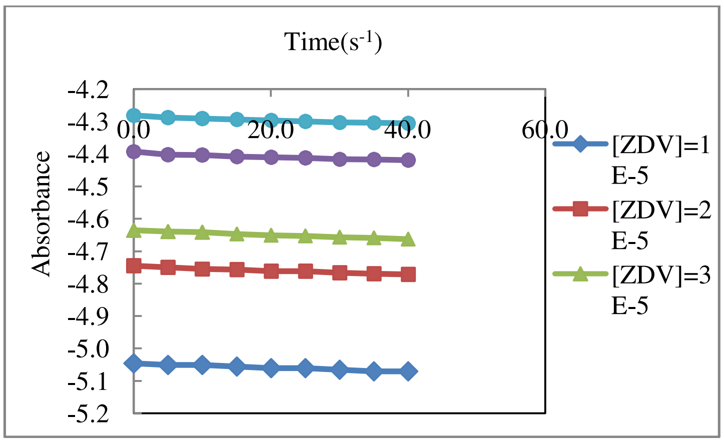

Figure-3
Graph showing degradation of Zidovudine with respect to time

Results and Discussion

The Analyses on rate of degradation of Zidovudine with reference to various parameters were conducted and the results are tabulated, graphs plotted and in depth discussion are carried out as follows:

Degradation studies of Zidovudine with variation of Drug: Concentration of drug [ZDV] was assorted from $1x10^{-5}$M to 6 $x10^{-5}$M for pH (3) and these two concentration are [HOCl] $=3x10^{-4}$M, [Buffer] = $6x10^{-3}$M. By following Beer Lambert Law graphs are plotted absorbance versus time shown in figure-3. Effect of variation of Zidovudine concentration of [$1x10^{-5}$] M to [$5x10^{-5}$] M with respect to time shows degradations at particular concentration. The degradation rate is not much fast. Maximum degradation are at concentration of ZDV=[$5x10^{-5}$] in pH 3. Zidovudine chemical reacts very less to chlorination process.

Variation of HOCl: Concentration of HOCl is assorted from $2.25x10^{-3}$ to $3.22x10^{-4}$ and remaining are kept constant for pH=3 and these two concentration are [ZDV] $=5x10^{-5}$, [Buffer]= $6x10^{-3}$. By following Beer Lambert Law graphs are plotted absorbance versus time shown in figure-4. Effect of variation of HOCl concentration of [$2.25x10^{-3}$] M to [$3.22x10^{-4}$] M with respect k'obs shows degradations at particular concentration. The plotting points lie on a straight line indicating linarity. k"app=1.496 $M^{-1}S^{-1}$ is the pH needy apparent second order rate.

Variation of Dielectric Constant: A cause of dielectric constant [D] was calculated through changeable the t- butanol water content within the reaction mixture in the company of all additional conditions are maintained steady like $[ZDV]=5x10^{-5}$ $[HOCl]=3x10^{-3}$ $[Buffer]=2x10^{-3}$. The solvent didn't respond in the company of the oxidant beneath experimental circumstances. The speed (rate) constant k'obs reduse in the company of reduce in the dielectric constant of the medium. The scheme of log k'obs against 1/D with points was linear with a negative incline and r^2 - 0.939 shown in figure-5.

Cause of Temperature: The speed of reaction was calculated next to three unlike temperatures with varying 10: 1 to 40: 1 $[HOCl]^o$ to $[ZDV]^o$ ratios by custody additional circumstances steady; the speed was originated to raise with raise in temperature. The second order speed constants k"app at three different temperatures 10, 25 and 35^{0}C were obtained. The energy of activation, Ea (51247.3kJ mol^{-1}) corresponding to these rate constants was evaluated from plot of log k" app against 1/T (r^2 > 0. 873) in addition to additional activation parameters $\Delta H^{\neq}$ (enthalpy of activation) (- 16874.9kJ mol^{-1}), $\Delta S^{\neq}$ (entropy of activation) (-365.3J K^{-1} mol^{-1}), $\Delta G^{\neq}$ (Gibbs energy of activation) (92013.3 kJ mol^{-1}) were calculated. Negative value of $\Delta S^{\neq}$ highlights the activated compound is higher ordered. Cause of temperature is shown in figure-6 and calculated results are tabulated in table-4.

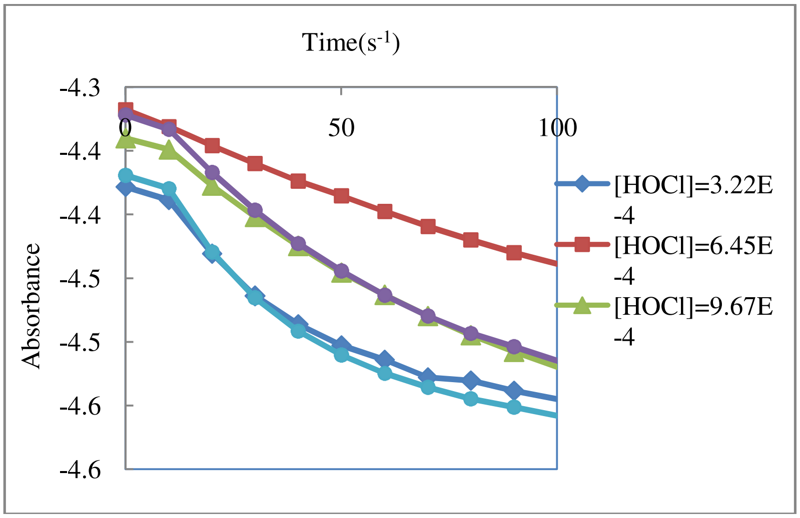

Figure-4
Graph showing the degradation at pH = 3 at various concentration of [HOCl]

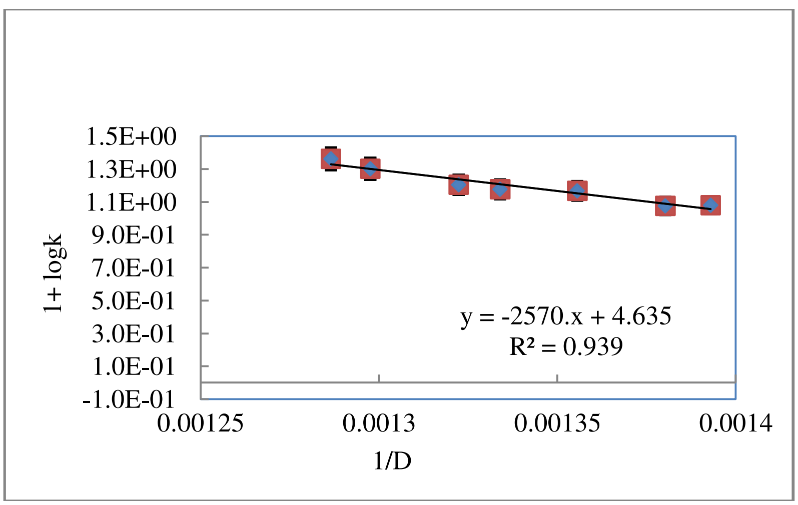

Figure-5
Effect of dielectric constant on the chlorination of zidovudine at 25 ^{0}C.Ionic strength = 0.02 mol dm^{-3} at 3 pH

Table-4
The above table shows Effect of Temperature on the rate of reaction

Effect of temperature on the rate of reaction						
Temp(kelvin)	**K**	**1/T**	**Logk**	**k/T**	**log(k/T)**	**logT**
283	8.08	0.003534	0.907411	0.028551	-1.54438	2.451786
298	2.47	0.003356	0.392697	0.008289	-2.08152	2.474216
308	2.47	0.003247	0.392697	0.008019	-2.09585	2.488551

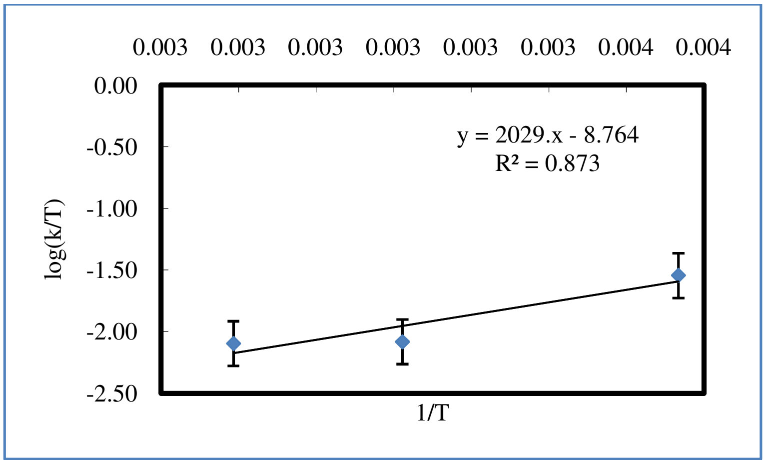

Figure-6
Effect of temperature on the chlorination of Zidovudine at 25 ^{0}C. 3 pH

Reaction Order: The concentration of ZDV was diversed in the choice 1x10^{-5} mol dm^{-3} to 2x10^{-5} mol dm^{-3} in addition to linearity plots of log [A_t-A_∞] Vs time (r ≥ 0.99) in addition to indicate a reaction order of accord in ZDV. A design of log k'obs versus log [HOCl]^o among 5 points was linear with a slope of 0.968 and r^2-0:992, indicating that this reaction can be treated as first order with respect to ZDV. The deliberation of HOCl was diverse in the choice 2.25 x10^{-3} mol dm^{-3} to 3.22x10^{-4} mol dm^{-3} and the graph of log k_{obs} Vs log [ZDV] is initiate to be linear by means of incline close to unity indicating unit order in HOCl. The reaction of ZDV with HOCl can be described as a bimolecular, second order reaction.

ZDV + HOCL → Product

Result of pH on the Reaction: The pH of the reaction mixture be varied from pH=3 – 8.8 by using acetate, phosphate and borate buffers, custody additional circumstances steady throughout experiment. The speed of degradation was established to decrease with increase in pH. Degradation did not take place for higher values of pH. Hence, the Zidovudine cannot be treated by conventional water treatment with chlorine.

Result of at first added products: At first added products such as chloramines or combined chlorine (CC) do not comprise some important result on the speed of reaction.

Discussions: Zidovudine reacts slowly with HOCl at oxidant concentration and pH conditions, which are similar to those likely to be observed in conventional water chlorination processes.From treatment perspective, pharmaceuticals be not odd natural chemicals plus their action taking away charge depend on the bodily and chemical properties of the drug composition. Predictable action processes with chlorination (free chlorine) be able to take out about 50 percent compounds, while advanced action processes, for example ozonation, advanced oxidation, activated carbon and membranes (e.g. reverse osmosis, nanofiltration), may be recommended to attain higher taking away charge, Reverse osmosis, such as, be able to take out additional than 99 percent of huge pharmaceutical molecules.

Degradation of Zidovudine decreases rapidly above pH 3. Hence conventional Chlorination cannot be applied for the removal of Zidovudine. Effect of Dielectric Constants on the rate constants of Zidovudine and HOCl reaction indicates the reaction involves dipoles and charged species. Effect of variation of Ionic strong point the speed of reaction indicates with intention of the effect is either between two neutral species or neutral and a charged species. The moderate value of $\Delta H^{\neq}$ (enthalpy of activation) and $\Delta G^{\neq}$ (Gibbs energy of activation) are both favorable for electron-transfer processes.

Conclusion

Zidovudine reacts slowly with HOCl at oxidant concentration and pH conditions, which are similar to those likely to be observed in conventional water chlorination processes. The rate of degradation of Zidovudine decreases rapidly above pH= 3 .Hence conventional Chlorination cannot be applied for the removal of Zidovudine. Effect of Dielectric Constants on the rate constants of Zidovudine and HOCl reaction indicates the reaction involves dipoles and charged species. Effect of variation of ionic strength indicates the reaction is either between two neutral species or neutral and a charged species. The moderate value of $\Delta H^{\neq}$ (enthalpy of activation) and $\Delta G^{\neq}$ (Gibbs energy of activation) are both favorable for electron-transfer processes.

Scope for Further Research Work: i. It is suggested to study systematically the kinetics and transformation pathways of antibacterial agents or antibiotics with disinfectants, such as ozone, permanganate, chloromines, etc during water disinfection process. ii. The rate constants have to be determined with varying dielectric constant viz, pH, temperatures and catalyst. iii. The study on degraded products of the aforesaid reactions can be studied using LC/MS study the on thermodynamic activation parameters for the reactions and finally can be taken up. iv. To study the environmental implications of the reaction have to be assessed.

References

1. http://en.wikipedia.org/wiki/Zidovudine **(2014)**
2. http://www.rxlist.com/retrovir-drug.htm **(2014)**
3. United States Pharmacopoeia (USP-NF XXIV), Rockville MD 20852. United States Pharmacopoeial Convention Inc, 3489 **(1985)**
4. Raviraj M Kulkarni ,Manjunath S Hangadakar , Ramesh S Malladi, Mahadev S Gudaganatti,Himansu S Biswal, Sharnappa T Nandibewoor., Transformation of linezolid during water treatment with chlorine – A kinectic study, *Indian Journel of Chemical Technology.*,(**21)** (38-43) **(2014)**
5. Marie Deborde, Urs von Gunten., Reactions of chlorine with inorganic and organic compounds during water treatment—Kinetics and mechanisms: A critical review, *Water Research.,* **(42)** (14) **(2008)**
6. Le-Minh N, Khan S.J, Drewes J.E, Stuetz R.M**.,** Fate of antibiotics during municipal water recycling treatment processes.,*Water research (***44)** (4296) **(2010)**
7. Mahadev S. Gudaganatti, Manjunath S. Hanagadakar, Raviraj M. Kulkarni, Ramesh S. Malladi and Rajaram K. Nagarale, Transformation of levofloxacin during water chlorination process: kinetics and pathways, *Progress in Reaction Kinetics and Mechanism*, **(37),** 367-368 **(2012)**
8. Sharada C.H., Channabasavaraj K.P. and Tamizh T., Mani, Development of a Spectrophotometric Method for the Quantitative Estimation of Zidovudine Concentration in Bulk and Pharmaceutical Dosage Forms, *KMITL Sci. Tech. J.*, **10(1),** 1-6 **(2010)**
9. APHA (American Public Health Association), AWWA (American Water Works Association).and WPCF (Water Pollution Control Facility), Standard methods for the examination of water and wastewater, *20th Edition,* Washington DC, USA **(1998)**
10. Basavaiah .K. and Anil Kumar. U R**.**,Simple Spectrophotometric methods for the determination of Zidovudine in pharmaceuticals using Chloramine-T, Methylene Blue and Rhodamine-B reagents, *E-Journal of Chemistry*, **3(12)**, 173-181 **(2006)**
11. Cimons, Marlene, U.S. Approves Sale of AZT to AIDS Patients, Los Angeles, (**1987)**
12. Dodd M.C. and Huang C.H., *Environ. Sci. Techn.,* **(38)**, 5607 **(2004)**
13. Gouthami K, Anusha Priyadarshini K, Nikhila Soundarya A, Pushpa Latha E**.**, Spectrophotometric Method For Degradation Study of Lamivudine**, (3),** 66-69 **(2013)**
14. World Health Organization International Agency For Research on Cancer, IARC Monographs On The Evaluation of Carcinogenic Risks To Humans, **(76)** 73-127 **(2000)**