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RELEASE STUDY OF ANTI CANCER DRUG, DOXORUBICIN FROM CARBON NANOTUBES

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ABSTRACT

Drug releases from nanoparticles to the site of action and subsequent biodegradation is important for developing a successful formulation. The present work is a prelude in the direction of using Carbon Nanotubes as a vehicle for drug delivery to the desired sites. Release study of the anti-cancer drug, Doxorubicin from the functionalized Carbon Nano tubes at different temperature and pH conditions was studied. Loaded anticancer drug shows better release in acidic medium. Moreover, increased release is seen with the increase in temperature.

KEYWORDS

Carbon Nanotubes, Anti-cancer drug, Doxorubicin, Release and Drug delivery.

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INTRODUCTON

Nanoscale materials can be used as drug delivery vehicles to develop highly selective and effective therapeutic and diagnostic modalities (McCarthy *et al*, 2005[1], Gao *et al*, 2004[2] and Langer *et al*, 2004)[3]. Small nanoparticles can circulate in the body and penetrate tissues such as tumors. In addition, nanoparticles can be taken up by the cells through natural means such as endocytosis. Nanoparticles have already been used to deliver drugs to target sites for cancer therapeutics (Gref *et al*, 1994) or deliver imaging agents for cancer diagnostics (Lemarchand *et al*, 2004)[4].

In general, targeted nanoparticles comprise of the drug, the encapsulating material and the surface

coating. The encapsulating material could be made from biodegradable polymers, dendrimers (treelike macromolecules with branching tendrils that reach out from a central core) or liposomes (spherical lipid bilayers). Controlled drug-delivery strategies have made a dramatic impact in medicine. Controlled release of drugs (such as small molecules, DNA, RNA or proteins) from the encapsulating material is achieved by the release of encapsulated drugs through surface or bulk erosion, diffusion, or triggered by the external environment, such as changes in pH, light, temperature or by the presence of analytes such as glucose (Langer *et al*, 2004)[3].

In spite of these advantages, nanoparticles do have limitations due to their small size and large surface area. This practical problems have to be overcome before nanoparticles can be used clinically or made commercially valuable.

Generally nanoparticles have relatively higher intracellular uptake compared to micro particles and available to a wider range of biological targets due to their small size and relative mobility. Drug release is affected by particle size. Smaller particles have larger surface area, therefore, most of the drug associated would be at or near the particle surface, leading to fast drug release. Whereas, larger particles have large cores which allow more drug to be encapsulated and slowly diffuse out (Redhead *et al*, 2001)[5]. Smaller particles also have greater risk of aggregation of particles during storage and transportation of nanoparticle dispersion. It is always a challenge to formulate nanoparticles with the smallest size possible but maximum stability.

MATERIAL AND METHODS

Drug Used

Doxorubicin

- Structure. (Figure No.1).
- Molecular formula: $C_{27}H_{29}NO_{11.}$
- Mol. Wt.: 579.99.
- M.P.: 204°C.
- Appearance: Orange red crystalline Powder, hygroscopic.
- Solubility: Soluble in water, slightly soluble in methanol.
- Storage: In air tight container.

Carbon Nano tubes (CNT): Procured from Monad Nanotech Pvt. Ltd.

RELEASE OF DOXORUBICIN- STUDIED AT DIFFERENT PH AND TEMPERATURE CONDITIONS

The release of Doxorubicin from CNT was studied under two different parameters i.e. pH and temperature. The range of pH studied were 2-14 whereas the range of temperature was 35-50^{0}C.

5mg of functionalized Multi walled Carbon Nanotube (f-MWCNT) loaded with drug was added to 10 ml of different pH buffers and the release study at different time interval was done at room temperature. Amount of released Doxorubicin was assessed by UV -Visible spectroscopy using calibration graph.

Release of drug from CNT was studied at different temperature conditions from 30^{o}C to 50^{o}C by adding 5mg of f-MWCNT loaded with drug to 10ml of buffer of pH 6 using precision water bath. Since, maximum release of drug was noted at pH 6.0, hence, even when the temperature varied the pH was kept constant at 6.

RESULTS AND DISCUSSION

Various methods that has been used to study the *in vitro* release of the drug are: (1) side-by-side diffusion cells with artificial or biological membranes; (2) dialysis bag diffusion technique; (3) reverse dialysis bag technique; (4) agitation followed by ultracentrifugation/centrifugation; (5) Ultra-filtration or centrifugal ultra-filtration techniques. Usually the release study is carried out by controlled agitation followed by centrifugation. In the present work drug release was not studied in living system. Rather efforts were made to record the drug release under pure chemical conditions.

In general, drug release rate depends on,

Solubility of Drug

Since MWCNT that was used is not water soluble and only Doxorubicin was water soluble; MWCNT was a good choice, as would not react with the

system. However, removal of MWCNT from the living system still poses a problem. Minimal use of CNT may not hamper the cellular system, as envisaged by Weismann (2003).

Desorption of the surface bound/ adsorbed drug

Is often pH dependent. Moreover cancerous cell are known to have different pH than normal healthy cells. Therefore, impact of pH on drug release was studied.

Release of drug in different pH conditions

It was found that the Doxorubicin starts getting released from CNT within an hour at all the pH; and release rate remains constant. In acidic pH with increase in pH value the amount of drug released increases whereas it slightly dwindles in alkaline medium may be due to slow dissociation of H-bonding.

As seen earlier the H- bonding interaction between Doxorubicin and CNT is strongest at neutral conditions i.e. pH 7, therefore release of drug is not seen in neutral conditions.

The release behavior at acidic and basic conditions may be due to partial dissociation of H- bonding.

Release of drug is almost double in acidic conditions compared to basic conditions. This may be due to the increased hydrophilicity and higher solubility of Doxorubicin at lower pH caused by increased protonation of $-NH_2$ groups on Doxorubicin, thereby reducing interaction between Doxorubicin and CNT.

Diffusion of Drug

Or in that matter any molecule through another matrix is a time dependent phenomena.

Impact of Time on Release of drug

Drugs attached MWCNT were found to start getting released within an hour of putting them into the release matrix. And after that it was almost the same even after 6 hours of release.

A histogram of % of drug released after different time interval is presented in (Figure No.2). If the diffusion of the drug is faster than matrix erosion, the mechanism of release is largely controlled by a diffusion process. It is evident that the method of incorporation has an effect on release profile. If the drug is loaded by incorporation method, the system has a relatively small burst effect and better sustained release characteristics (Fresta *et al*, 1995)[6]. Whereas, if the drug is attached to the surface or adsorbed to the surface, the release is then controlled by diffusion of the drug.

Moreover, diffusion is also affected by the temperature.

Therefore Impact of different temperature on Release of drug - from CNT was studied. The temperature studied were 30^{o}C to 50^{o}C using precision water bath in buffer of pH 6, because at this pH maximum release was seen (Table No.4).

Degradation of Nanoparticle after Drug Release

Nanocarbon being an inert material in absence of light, do not degrade in chemical or living system. However, very high acidic pH do tend to damage the surface of CNT. In the present work the MWCNT after the release of drug even at pH 2 did not show any surface damage. Therefore, it is imperative that very short lengths of MWCNT should be used as drug carrier, so that it can be excreted from the system.

Thus solubility, diffusion and biodegradation of the matrix materials, if used, govern the drug release process.

Table No.1: Absorbance at 490 nm of the released amount of drug at different time intervals at room temperature (27^{o}C)

S.No	Time	pH 2	pH 4	pH 6	pH 7	pH 9	pH 11	pH 14
1	1 hrs	0.081	0.079	0.086	0.0	0.042	0.037	0.049
2	3 hrs	0.081	0.079	0.086	0.0	0.060	0.045	0.049
3	5 hrs	0.081	0.079	0.086	0.0	0.060	0.060	0.049
4	6 hrs	0.081	0.079	0.086	0.0	0.060	0.060	0.049

Table No.2: Corresponding Concentration of Doxorubicin in mg/ml by calibration graph

S.No	Time	pH 2	pH 4	pH 6	pH 7	pH 9	pH 11	pH 14
1	1 hrs	0.0235	0.023	0.025	0.00	0.012	0.0105	0.014
2	3 hrs	0.0235	0.023	0.025	0.00	0.0175	0.013	0.014
3	5 hrs	0.0235	0.023	0.025	0.00	0.0175	0.013	0.014
4	6 hrs	0.0235	0.023	0.025	0.00	0.0175	0.013	0.014

Table No.3: Percentage release of Doxorubicin (5mg of f-CNT contains 0.08 mg of Doxorubicin loaded, hence percentage release was calculated)

S.No	Time	pH 2	pH 4	pH 6	pH 7	pH 9	pH 11	pH 14
1	1 hrs	29.38	28.75	31.25	0.00	15.0	13.13	17.5
2	3 hrs	29.38	28.75	31.25	0.00	21.8	16.25	17.5
3	5 hrs	29.38	28.75	31.25	0.00	21.8	16.25	17.5
4	6 hrs	29.38	28.75	31.25	0.00	21.8	16.25	17.5

Table No.4: Percentage release of drug at different temperature conditions

S.No	Temperature	Drug Released
1	30 ^{0}C	31.25%
2	35 ^{0}C	32.5%
3	40 ^{0}C	33.13%
4	45 ^{0}C	33.75%
5	50 ^{0}C	33.75%

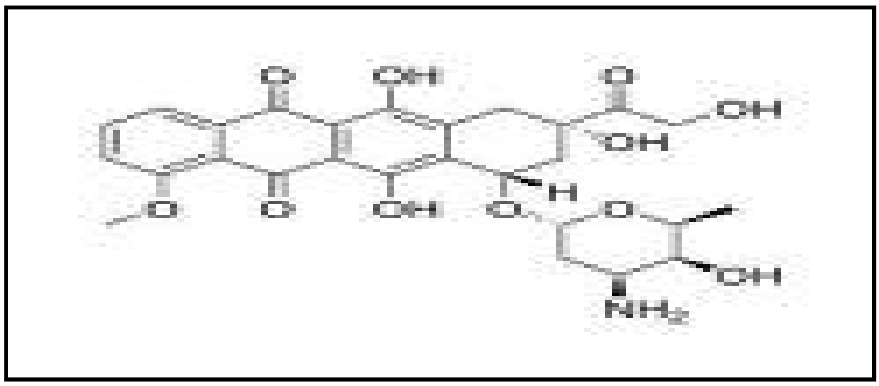

Figure No.1: Structure of Doxorubicin

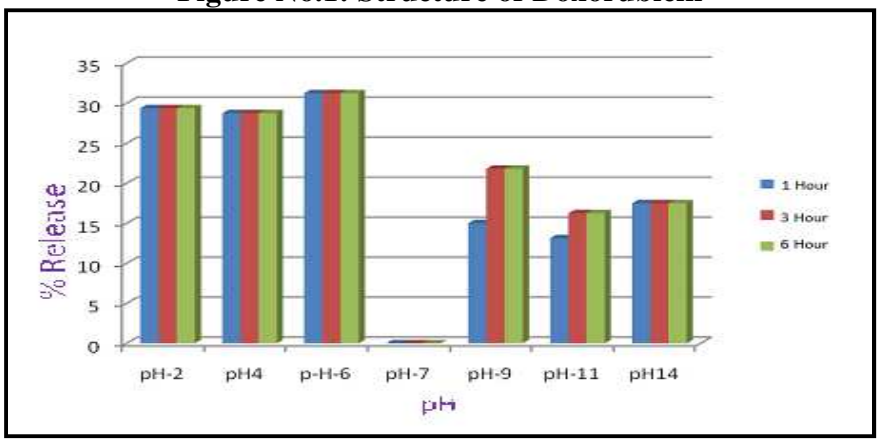

Figure No.2: Graph of % release at different time interval *Vs* pH

CONCLUSION

Carbon Nanotubes (CNTs) have emerged as a recent and promising option especially in cancer therapy. Loaded anticancer drug shows better release in acidic medium. Moreover, increased release is seen with the increase in temperature.

To optimize this drug delivery system, greater understanding of the different mechanisms of biological interactions, and particle engineering, is still required. The present work is an initial effort in this direction.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBILIOGRAPHY

1. McCarthy J R, *et al.* "Polymeric Nanoparticle Preparation that Eradicates Tumors", *Nano Lett,* 5(12), 2005, 2552-2556.
2. Gao X, *et al.* "*In Vivo* Cancer Targeting and Imaging with Semiconductor Quantum Dots", *Nat Biotechnol,* 22(8), 2004, 969-976.
3. Langer R and Tirrell D A. "Designing Materials for Biology and Medicine", *Nature,* 428(6982), 2004, 487-492.
4. Lemarchand C, *et al.* "Polysaccharide-decorated Nanoparticles", *Eur J Pharm Biopharm,* 58(2), 2004, 327-341.
5. Redhead H M, Davis S S, Illum L. Drug delivery in poly (lactide-co-glycolide) nanoparticles surface modified with poloxamer 407 and poloxamine 908: *Mohanraj and Chen* 572, *Trop J Pharm Res,* 5(1), 2006. *In vitro* characterisation and *in vivo* evaluation, *J Control Release,* 70(3), 2001, 353-363.
6. Fresta M, Puglisi G, Giammona G, Cavallaro G, Micali N, Furneri P M. Pefloxacin mesilate- and ofloxacin loaded polyethylcyanoacrylate nanoparticles; characterization of the colloidal drug carrier formulation, *J. Pharm. Sci,* 84(7), 1995, 895-902.

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