EMPLOYMENT OF PHOTORESPONSIVE POLYMERS IN DRUG DELIVERY AND THERANOSTICS TECHNIQUES

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ABSTRACT

Polymeric nanoparticles (NPs) as a novel drug delivery systems (DDS) possess so many advantages over typical carries, NPs retain into site of actions adequately with an extra specificity due to their passive (NPs retention through enhanced permeability retention (EPR) effect) and active targeting (Can attach one of ligands to binds special tissue molecules). Very recently, researchers have been more concerned about stimuli responsive; that achieved when Polymers attached to stimuli molecules as the Ultraviolet light (UV) responsive moiety Spiropyran (SP). SP modulate polymeric system to deliver load only when UV triggers SP structural changes lead to DDS release i.e. polymer-SP system would carry drugs intact especially in cancer therapy where premature release is truly an immense burden to overcome.

KEYWORDS: Polymeric Nanoparticles, Solid Nanoparticles, Photoswitches, Spiropyran, Merocyanine, Photoresponse.

1. INTRODUCTION

Many attempts to construct novel drug delivery systems have achieved timecontrolled and site-specific targeting of therapeutic agents just during the last decades concerning diseases control. That effort improves remarkably the efficacy of drug thus minimize undesirable side effects of various illnesses even though some hurdles as cancer with its remarkable complexities- has become a very disastrous disease that challenges the scientists all over the
world to overcome.\textsuperscript{[1-4]} Such anticancer difficulties as resistance, uncontrolled targeting, solubility within the circulation and premature release of carriers\textsuperscript{[5,6]} however through taking the advantage of smart delivery and concomitant diagnostic properties of such approaches also have been examined and to this point gave worthy results considerably.\textsuperscript{[2,7,8]} Another complexed disease is Alzheimer (AD) likewise is among the top of the list, it episodes suddenly due to the difficulty with early diagnosis and blood-brainbarrier obstacles.\textsuperscript{[9,10]}

Many of novel drug delivery systems gave well to excellent responses up to now. Self-assembled nanostructures; liposome, dendrimer, micelle, and artificial deoxynucleic acid (DNA) considered among the list.\textsuperscript{[11]} Nevertheless, many of them are still facing boundaries of how to direct the drug load to its intended site within the desired time i.e. most of them lack the as time and site control release smart dosage forms and to give pulsatile release states according to the rhythmic behavior of symptoms.\textsuperscript{[4,12,13]} One of such smart approaches is responsive dosage forms. Internal stimuli-responsive dosage forms benefit from the internal environment of tumor cells such as pH differences, redox potentials variations, and enzymatic status deference while external stimuli depend on triggers that initiated from outside body such as thermal, near infrared, ultrasound and light responsive drug delivery systems (DDS).\textsuperscript{[4,14]}

Spiropyran (SP) is a chromophore belongs to azobenzines molecules, is ultraviolet (UV) responsive moieties with highly promising outputs which under specific UV wavelengths irradiation SP chromophores attain some chemical and physical rearrangement (Dynamic remodeling)\textsuperscript{[15,16]} and that releases drug load within the delivery system - as micelles- in the precisely acquired time and site.\textsuperscript{[1]}

\begin{center}
\begin{figure}
\includegraphics[width=\textwidth]{spiro.png}
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2. Photoresponsive Molecules

Generally speaking, various photoswitchable molecules – Azobenzines stilbenes, Spiropyran, diarylethenes, fulgides and others have been widely focused on and involved in the assembly of light-responsive systems and materials, each of those photoswitches has its benefits and
drawback that needs some extra modulation to optimize their photochromic attitudes.\textsuperscript{[1,14,17]} SP is among most photoswitches that frequently studied and this mainly cause of the reversible isomerization character; the colorless hydrophobic SP upon UV irradiation in specific wavelength turns into the colored hydrophilic Merocyanine isomer (MC), this reaction can be reversed by visible light that gave SP its prevalent applicability.\textsuperscript{[18,19]}

3. Isomerization of Spiropyran
Photochromic modules when mentioned they refer to those materials undergo structurally and color changes upon specific wavelength irradiation, meantime this color transaction is visible-light reversible giving the original substrate again\textsuperscript{[20]}, furthermore this property aids to exploit such compounds in numerous new responsive dosage forms, imaging, diagnostics, besides other photoresponsive materials.\textsuperscript{[16]} Spiropyran was first discovered since a long time around 1921, but it took a while for their chemical and dynamic properties to be extensively understood, their photochromism remained unexposed until 1952 by Fischer and Hirshberg\textsuperscript{[21]}, and for extended periods they are being regularly examined for their photodynamic isomerization but still those dynamics recall such a huge concerns.\textsuperscript{[22]}

As a dynamic material, SP units should follow covalent fusion to materials of a delivery system (macromolecules or surfaces) while the capability of noncovalent bondage is another choice but contain many drawbacks as SP units could easily dissociate prematurely.\textsuperscript{[23]}

The molecule includes an indoline and a chromene structures bonded together by a Spiro-junction perpendicularly, SP when irradiated with UV, the SP heterolytic C–O bond cleaves to via an opening ring reaction that terminates with the colored hydrophilic MC.\textsuperscript{[22-24]}

4. What make SP-MC dynamic characteristics particularly unique?
Photochromic properties discussed a long time ago with different chromophores who responds to diverse light waves however and they share some major aspects but SP holds some distinctive features (Table 1).

The extensive value of the Spiropyran switches realizes mainly since the SP and MC isomers have infinitely different physicochemical properties under UV light irradiation. Charge variation in MC generates an intense polarity compared to SP isomer. SP and MC attain a substantial structural difference which makes SP inhabits less volume than MC. Furthermore, SP isomer does not absorb visible light (near infrared NIR) whereas MC absorbs strongly at
max wavelength = 550-600 nm and appears deep blue.\textsuperscript{23,25,26} Hence, all that mentioned guarantee a prominent mechanical response within the delivery model and when happens, those rearrangements release the load with distinguishable fluorescence changes.

SP photochromism has undergone excessive endeavors to study influence of such various stimuli, most of that efforts have challenged a lot to formulate smart novel responsive delivery structures that exert precise time transport and site targeting not only as photoresponsive but also SP-MC isomerization can be attained through other responses such as thermoresponsive\textsuperscript{27}, redox-responsive\textsuperscript{28,29}, potential hydrogen (PH) responsive.\textsuperscript{30,31} It’s also proved that SP molecule could easily get conjugated covalently or non-covalently\textsuperscript{32} to various moieties like polymers and active ligands which what makes SP greatly and easily modifiable to form so many drug delivery systems.

5. SP-based novel drug delivery systems (DDS) conjugates and SPco-polymerization

As mentioned beforehand the photoresponsive nanoparticles are prepared through either physical adsorption or covalent bondage to combine the Chromophore into the vehicles. Usually, the delivery that loads drug inside circulation or orally faces problems of solubility, premature drug cargo release before reaching release site, besides targeting itself considered a huge difficulty especially in chemotherapy, polymeric delivery as other novel intervention in DDs.\textsuperscript{1} SP can be incorporated within different delivery surfaces; with polymers\textsuperscript{3,17,33}, metallic ions\textsuperscript{34} or it could be adsorbed on other surfaces as with silica and carbon surfaces.\textsuperscript{35,36} Two strategies are predominant for attachment, one is by direct Co-polymerization of SP monomers to construct up larger united structures and this choice hadn’t been examined broadly until recently (Suhyun Son, et al; 2014) who they polymerized SP along with hyperbranched polyglycerol (SP-HPPG) that ultimately had been formed into micelles.\textsuperscript{37}

The second approach is via utilization of the reactive moieties of SP to bind covalently to polymers via reacting the SP with the side chain of that polymer.

This considered the best choice ever found to this point.\textsuperscript{38} This kind of covalent conjugates assure stability of the nanoparticle system and its tight delivery unlike SP polymerization, which can produce premature release and needs more characterization processing that assures the polymeric system is stable before and after micelle preparation, that drawback is not in covalently bonded conjugates.
5.1 SP-based micelles: Greater interests all through have been devoted on investigating stimuliresponsive dosage forms that controllably release active cargo to its anticipated site within controlled timing, block copolymers (BCP) micellization with.

Table 1: SP and other UV light responsive chromophores main useful characters.

<table>
<thead>
<tr>
<th>SP Characteristics: UV light photoresponse That reversed by Vis-light</th>
<th>Useful utilizations</th>
<th>Rewards of SP over other chromophores</th>
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<tbody>
<tr>
<td></td>
<td>UV light makes SP ring (hydrophobic) to open up producing the isomer MC (hydrophilic) which mask many hydrophobic drugs\cite{23,39}</td>
<td>300-400 nm UV light is fairly harmless, feasible, and reversible, UV waves are more controllable compared to other external stimuli i.e. thermal, ultrasonic</td>
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<tr>
<td>prospect of multi-stimuli: pH, redox, and thermos-responsiveness</td>
<td>Exploit the differences between internal – mostly tumor -microenvironment and surroundings (internal; PH and redox potential ) besides external like thermos-response\cite{40,41}</td>
<td>The Possibility of multistimuli responses can be examined jointly and comparatively</td>
</tr>
<tr>
<td>Covalent attachment capability</td>
<td>polymers in a system are Strongly attached covalently to SP via numerous functional groups\cite{19,42,43}</td>
<td>Benefits in vehicle solubility, reduced photodegradation, prevent MC clump to the backbone, augment biocompatibility. All that creates an exceedingly punctual controlled system\cite{23,54}</td>
</tr>
<tr>
<td>Capability of imaging</td>
<td>Could be linked to bio-targets for microenvironment analysis, either directly by using SP fluorescence or via biological probes\cite{9,23,43,45,46}</td>
<td>Th i s g i v e s w a y for earlier insights on such unobtainable conditions when peptides are involved as kinases phosphorylation and Alzheimer disease</td>
</tr>
<tr>
<td>Other chromophores</td>
<td></td>
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<tr>
<td>Azobenzines</td>
<td>Undergo UV trans-cis photo isomerization give NP that can engulf both hydrophobic and hydrophilic drugs\cite{15,47}</td>
<td></td>
</tr>
<tr>
<td>Diazo-Naphthoquinone (DNQ)</td>
<td>Reacts to UV/NIR by Wolf rearrangement converts into hydrophilic 3-indenecarboxylic acid (3IC) and other esters that also might help in UV/NIR photoresponse\cite{48,49}</td>
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</table>

chromophores that under light irradiation lead to spontaneous load release with the controlled site and time reflected objectively enhanced release profiles especially in cancer.\cite{50}

Micelles are colloidal units that vary in size but usually, the range is 5–100 nm Nano-particulate properties. They show greater promises as carriers for hydrophobic loads beside, its passive delivery as nanoparticle system. Micelles efficiently are able to be fused to targeting molecules that directed to attach at particular cellular receptors, they are easy to be modified with numerous stimuli for instance; ultrasound and light (external stimuli) while
(PH), oxidative stress potential (internal stimuli) all of above are responsive release micellar systems\textsuperscript{[51]} (Table 2).

Undeniably, polymeric micelles considered as an ideal nanocarrier technique especially for anticancer delivery for diverse rewards. Their small nanoparticle size manages them to stand in circulation longer. Also, acquire them a well-modulated release characteristic of drug load within the core (lipophilic drugs are usually most drugs take benefit of this property) or attached within micelles hydrophilic tails for hydrophilic drugs.\textsuperscript{[29]} That property is highly needed to enhance bioavailability meanwhile aids in masking immune response of natural products. SP-based block copolymer (BCP) micelles are the most light- triggers that had been fabricated and inspected to this point considering Spiropyran unique ultraviolet (UV) light transformation characteristics which attain SP to be joined to different polymers with different ways.\textsuperscript{[17]}

Fabrication of polymeric DDS with various diameters of SP conjugated micelle models had successfully encapsulated model drugs and released them efficiently. (Table 2) active targeting is possible by using some kinds of targeted macromolecules/and moieties such as hyaluronic acid which recognizes CD\textsuperscript{[44,42]} the well-known cell Penetration peptide (tLyP-1) is another model that bind the transmembrane protein NRP1 (neuropilin 1) co-receptor in some tumors types 5 also an example to active micellar delivery.

5.2 SP-based Vesicles: Vesicles spontaneously formed when amphiphilic polymers found in a hydrophilic media as a matter to reduce excess water–hydrophobic interfaces under specific pH via some preparation techniques with sizes of 5-30 nm,\textsuperscript{[52,53]} sometimes those polymeric copolymers retain so many stylish structures of bulky, short worms, end cap defects and Y-junction are all vesicular designs.\textsuperscript{[54]} Vesicles considered well-adapted theranostics (contain both drug delivery with imaging ability) hence gave very good outcomes,\textsuperscript{[55]} particularly for anticancer and genetic materials delivery.\textsuperscript{[56,57]}

There are so many ways to do vesicles nevertheless, the more simple and achievable is what so-called polymerization induced self-assembly and reorganization (PISR)\textsuperscript{[58,59]} had become a common approach to formulate vesicular polymerosomes. SP optically- elicited vesicles had been examined with good outcomes though hadn’t been investigated that much as micelles however fair enough disintegration of the vesicular copolymer models had been noticed after they got modified with SP.\textsuperscript{[52,59]}
Table. 2: Some of Sp-based micelles responses to UV/vis light.

<table>
<thead>
<tr>
<th>Micelle system</th>
<th>Change after UV/Vis light</th>
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<tbody>
<tr>
<td>Micelles of Tri-block copolymer (EC-g-PHEMA-g-PSPMA)</td>
<td>365 nm reduced micelles diameter from 84.6 nm to 73.2 nm. 620 nm Vis-light/30 min, 150 min increased diameters to 83.3 and 85.2 nm respectively.(^{[3]})</td>
</tr>
<tr>
<td>Tri-block copolymer of SP-hb-PG With 33.2 ± 11.8 nm</td>
<td>Micelles of 33.2 ± 11.8 nm under 365 nm/30 min reduced to about 0.1 nm 620 nm Vis-light/30 min induced aggregation of micelles to about normal diameter.(^{[37]})</td>
</tr>
<tr>
<td>Block copolymer of PEG-b-PSPMA</td>
<td>365 nm UV irradiation/5, 10 min changed diameters to 132 nm, 87 nm respectively. Started from 87 nm, 550 vis-light/20 min, 40 min, 1 hr. Diameters increased to 110 nm, 130 nm, and 157 nm respectively.(^{[33]})</td>
</tr>
<tr>
<td>Poly((±)-(endo,exo)-bis[6- (30,30-dimethyl-6-nitrospiro- [chromene-2,20-indolin]-10-yl) hexyl] bicyclo[2.2.1] hept-5-ene-2,3-dicarboxylate)</td>
<td>Diameters changed from 106.0 ± 13 to 91.9 ± 0.5 nm after 365 nm UV light, Vis-light of 572 nm increased diameters up to 105.4 ± 1.4 nm which is close to normal size 18</td>
</tr>
<tr>
<td>Spiropyran-based random Copolymer P(SPMA-co-DMAEMA) micelles</td>
<td>After spontaneous micelles formed, visible light turn them into hydrophobic and precipitated in deionized water (SPMA is hydrophobic on vis-light and hydrophilic in UV).(^{[19]})</td>
</tr>
<tr>
<td>PC-SPMA micelles</td>
<td>A fluorescence peak recorded at 534 nm (MC peak) after UV light indicating system destruction.(^{[41]})</td>
</tr>
<tr>
<td>mPEG-b-poly(Tyr)25-SP micelles</td>
<td>After UV light/10 min, system beaked at 550 nm as MC formed, micelles diameter also decreased as well.(^{[60]})</td>
</tr>
</tbody>
</table>

Abbreviations: P(SPMA-co-DMAEMA): poly(dimethylamino ethyl methacrylate-co-Methacrylic acid) Spiropyran 2-(dimethylamino) ethyl methacrylate. PC-SPMA: Pluronic chitosan poly(dimethylamo ethyl methacrylate-co-Methacrylic acid) Spiropyran. mPEG-b-poly(Tyr)-SP: poly(ethylene glycol)-modified poly(poly(a hydroxy acids)).

### 5.3 SP-based Liposomes
Phospholipid when retained into bilayer enclosure long ago provided attention not only to carry lipophilic drugs but also proved imaging likelihood concomitantly.61 Photoswitches modifiable bilayers affect ions transportation across various cellular membranes acquire genetic materials- liposomal delivery when accompanied to tumor-specific stimuli such as pH trigger,\(^{[39,62]}\) furthermore; Antibodies, ultrasonic, magnetic and electric targeting molecules are similarly attachable to liposomal systems.\(^{[63,64]}\)

UV/vis light exposure have shown various impacts on anionic /and zwitterionic SP-liposomal membranes ultimately influenced liposomal disarrangement and reformulation reversibly that gives chance to tightly controlled drug delivery.\(^{[65,66]}\) Targeted ligands have been also examined using a dual emulsification of targeting peptides and non SP-photoswitches peptides of specific sequences that were triggered by near infrared light when liposomes reached the projected site.\(^{[67]}\)
5.4 Spiropyran conjugated silica brushes: Lately, silica as inorganic solid nanoparticles (SiO₂, SNPs) has excessive attention as drug-carrier’s that is because they possess huge surface of hydroxyl moieties that enable it to higher and easy functionalization.\[2\]

Moreover, silica NPs surfaces attain to form polymer brushes, a thing achieved via merging moieties (organic and inorganic) to silica surfaces covalently. Such an approach to modify silica surfaces was noticeably demonstrated in (Hui Liu, et al; 2016) work. They coated Silica SNPs with PH responsive polymer Methacrylic acid (MAA) and chromophore Spiropyran P(SPMA-co-MAA),\[68\] and once UV irradiated, the average diameter increased from 185.7 to.

212.7 indicating chromophore has aggregated in the hydrophilic media after SP-MC polymerization. Such systems get benefit of both SiO₂ surfaces plus UV-response.

5.4 In vivo imaging, tracking, and real-time disease monitoring: Applications of inorganic metals who act as theranostics studied for so long with, they gave enhanced imaging yields to a larger extend\[69,70\] but then again, metals nanoparticles have their own cons and pros but in so many cases lack biocompatibility and possess higher toxicity.\[71,72\] Polymeric nanoparticles have become utilizable in favor of biocompatibility, retention time to the site of actions, and they can be widely modified with external and internal stimuli.\[73,74\] photoresponsive-based imaging unwrapped barriers to expose biological mechanisms in real time regardless of the so many restrictions of typical imaging processes.\[75\] This comprehended when SP moieties conjugated to special tags who accurately target tumor microenvironment reacting with tumor markers so offering an essential technique for parallel observation of diseases moreover it possesses numerous compensations; cheaper, zero radioactivity disclosure and its comparative handling convenience all considered encouraging benefits.\[76,77\] The therapeutic procedure as nanoparticle smart delivery has recently come to be more collaborative. A possibility of parallel observation from the time of ingestion of drug to the body, passing through body compartments, and until it is cleared out has become very conceivable presently.\[78,79\] Fluorescence resonance energy transfer (FRET) represents an applicable technique to track the drug fluorescently giving real-time drug observation.\[33,80,81\]

Many new approaches towards continuous disease nursing in earlier phases had offered many insights with SP photodynamic. The SP modified fused-silica ducts are able to act as integrated optical sensors for continuous flow analysis,\[82\] this SPoptical sensor technique
allows spotting of such diseases that considered for decades obstacles allowing very early identification. The establishment of soluble B-Amyloid oligomers plaques correlated badly to deterioration of AD than the insoluble plaques, once some fluorescent approaches these plaques; it may breakthrough earlier AD detection. A conjugate system of SP-MCAminonaphthalene 2-cyanoacrylate (ANCA) created by (Guanglei Lv et al; 2016), crossed brain and reacted with a soluble site of B-Amyloid giving an anticipation for very early recognition.\textsuperscript{[9]} In addition to micelles and drug conjugates, liposomes, vesicle, and nanotubes likewise examined vigorously for imaging competences with several fluorescent moieties such as fluorescein isothiocyanate, distearoylphosphatidyl-ethanolamine (DSPE).\textsuperscript{[79,83]}

6. Release profile within different SP-based Nano-formulations
Micelles are more competent compared to other conducts of Nano-delivery. Micelles easily can formulate nanoparticulate structures along with a capability of attaching numerous targeting molecules all had dragged an attention as polymeric nanoparticles.\textsuperscript{[73]} when micelles become stimuli-responsive that enhances their release parameters greatly\textsuperscript{[60]} However, on the other hand, enhancement of hydrophobic loads is promising similarly with responsive systems other than micelles, for example liposomes, vesicles and nanotubes though they.

<table>
<thead>
<tr>
<th>Photoresponsive Systems</th>
<th>Release Profile</th>
<th>References</th>
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<tbody>
<tr>
<td>Amphiphilic micelles with Coumarin as model drug</td>
<td>Started with 0.1 mg of coumarin* as an initial concentration; fluorescence peak of emission decreased gradually with time of UV-light irradiation, and emission reduced steadily also with Vis-light</td>
<td>[60]</td>
</tr>
<tr>
<td>Amphiphilic copolymer of PEG-SPMA with NBD as model drug</td>
<td>Upon UV-light, NBD-loaded micelles changed in color from orange to red indicating NBD release</td>
<td>[33]</td>
</tr>
<tr>
<td>(HPHEEP-OH)-SP micelles</td>
<td>Coumarin 102 model drug after UV irradiation exhibited strong emission peeks (micelles disintegrated and dye released), the status reversed by VIS-light</td>
<td>[1]</td>
</tr>
<tr>
<td>Adhesive Nanoparticles GO-HA-SP got use Of both UV photoresponse and pH Of cancer cells</td>
<td>DOX loaded onto surfaces via π−π and hydrophobic interactions; followed UV fragmentation of adhesive -based GO system then, acidic pH leads to release up to 50% and 90% within 24 and 48 hrs. respectively</td>
<td>[42]</td>
</tr>
<tr>
<td>(SP-hb-PG) micelles</td>
<td>Pyrene dye** under UV irradiation emitted peaks that steeply fell to baseline during deferent time’s intervals from 5-30 minutes that insure micelles deformation and Pyrene release. Intensity of excitation peaks increased with Vislight.</td>
<td>[37]</td>
</tr>
<tr>
<td>Triblock copolymer micelles of (EC-g-PHEMA-g-PSPMA)</td>
<td>Under UV-light, micellar system reflected considerable release of Pyrene compared to that when Vislight Irradiated</td>
<td>[3]</td>
</tr>
</tbody>
</table>
Notes: * and ** are dyes that become more soluble in hydrophobic media i.e. upon SP presence so they emit more after vis-light irradiation (re-encapsulation).

Abbreviations: PEG-SPMA, poly-ethylene glycol-Methacryloxyethyl-SP; NBD, Nitrobenzofurazan; HPHEEP-OH, Hydrophilic hydroxyl-capped –hyperbranched polyphosphate; GO, Graphene Oxide; DOX, Doxorubicin hb-PG, Hyperbranched polyglycerols; EC-g-PHEMA-g-PSPMA, Ethylcellulose-g- poly (2-hydroxyethyl methacrylate)-g-poly(Spiropyran ether methacrylate). need extended studies. The literature showed considerable SP-DDS responses of various polymeric designs who gave worthy effects of targeting different loads (Table 3).

7. Challenge of UV-light tissue penetration weighted to tissue toxicity: Ability of UV light to influence photoresponse sometimes it could conflict with tissue toxicity concerns and load delivery on the other hand,[84,85] such a thing had pulled back most of work to employ chromophores in drug control field nonetheless many studies demonstrated that UV-waves on range of 300-400 nm - those ranges to trigger SP-MC conformational changes- is hugely safe. In addition, UV-light if irradiated locally on such cancer sites need to be treated; this value could reduce probability of harming non-cancerous tissue impressively. It is true that animal data showed reasonably penetration results, but reproducibility of clinical use of this style waits to be confronted extensively as the human body has extra complexities of barriers to this range of UV waves.[4] The laboratorial difficulties during treatment also needs special considerations.[2]

8. CONCLUSION AND PROMISES

NPs had become very concrete aspect of drug delivery, serous disease require serious ways of fighting, cancer cells for instance due to their special environment which created to maintain prosperous living parameters, they resist antitumor drugs with their rapid genetic mutations leads to either efflux of drugs out of tumor cells or drugs become inactive cause of cancerous cells. Another thing arise here as so important is the targeting problems of conventional anticancer drugs, they can’t in most of the cases to differentiate between normal and cancerous cells so there is a liability of intensive side effects need to manage. Targeting of NPs based DDS ability relived some of that stress off oncologists and cancer management specialists, it becomes possible to load anticancer drug precisely intact to its targeted site. The likelihood of responsive DDS to affect the time when loads will be released -after attaching
specific responsive moieties to the DDS-, that realized what researchers dreamed of, the so-called “brute-force” for cancer therapy.

Light responsive DDS although not yet employed to control delivery let us say on clinical wise aspects but at least on a research scale they gave promising outcomes to manage such shortages of conventional delivery. UV light as a source of a responsive trigger to release loads has met some worries, such of which is the harm to living cells. Luckily, studies assured that UV light in the safe range of 300- 400 nm is capable of affecting several chromophores -like SP-, which securely can construct light responsive DDS. With all that mentioned rewards, SP could be promising to form many NPs based systems for clinical application, especially in cancer therapy region.

9. CONFLICTS OF INTEREST
The author reports no conflicts of interest in this work.

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