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Photopharmacology

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Abstract **Review Article**

Photopharmacology means use of light to precisely drug deliver at target site. Such a novel methods ability to improve drug specificity by reducing off-target effects. The energy of light is used to change for shape and chemical properties of the drug, resulting in different mechanism of action of drug. This is done to eventually to get control when and where drugs are active in a reversible manner, to prevent side effects, Adverse effects, and toxicity. It aims to reduce systemic toxicity of drug and the emergence of resistance, while attaining unprecedented correctness in treatment. Azobenzenes, the little photoswitches that could' - very reliable little engines with which to drive things." The steadier *trans* isomer has the benzene rings on reverse sides but, on radioactivity with ultraviolet (UV) light, this switches to the *cis* verification, with the benzene rings sitting next to each other. Azobenzenes also advantage from being a large pre-existing list of toxicity data owing to their extensive industrial use. A novel drug Glimethoride is a third-generation sulfonylurea, consist of an azobenzene unit. The drug activated after a meal, most probable using an implanted blue LED: "The drug switches on very rapidly in milliseconds, and because it switches off within about two seconds and able to get quite fine control. Photopharmacology could also be used to target antibiotic resistance. It has been novel research in the field, has decades of knowledge in designing molecular switches for nanoelectronics and saw a prospect to try some of that experience to the problem of antibiotic resistance.

Keywords: Photopharmacology, Photoswitches Azobenzenes, Glimethoride.

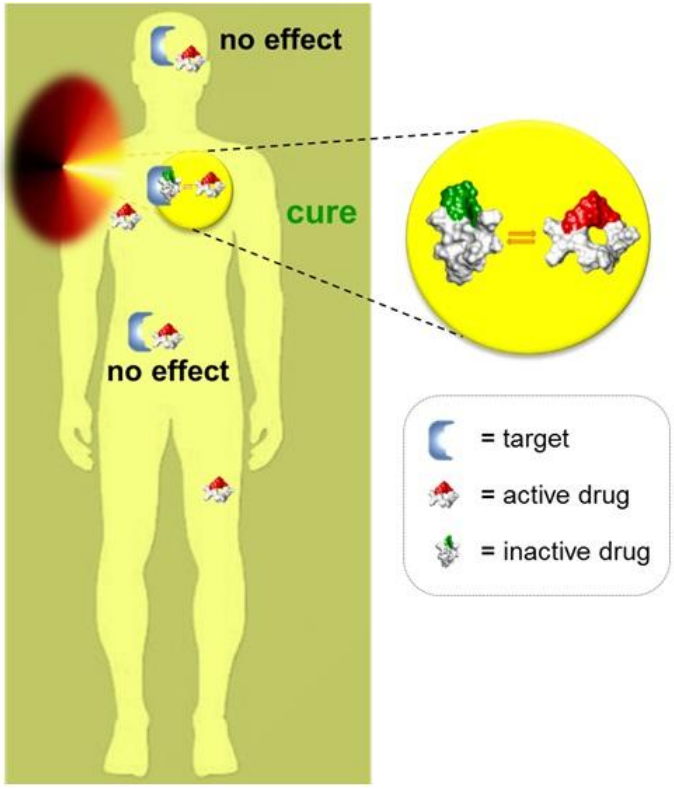
INTRODUCTION

Photopharmacology means use of light to precisely drug deliver at target site. Such a novel methods ability to improve drug specificity by reducing off-target effects [1]. The energy of light is used to change for shape and chemical properties of the drug, resulting in different mechanism of action of drug. This is done to eventually to get control when and where drugs are active in a reversible manner, to prevent side effects, adverse effects, and toxicity [2]. Selectivity to target site/organ can be augmented by various approaches and photopharmacology is one such approach. Photopharmacology give us an external photoswitch to manage off-target site drug action, and thus helps to reach selective target action and alleviate off-target toxicity and resultant side effects. [3] Selectivity to target tissue/site is a problem with most of the drugs; most of the sites of actions of drugs (receptors, enzymes, ion channels, and carrier molecules) are expressed in other sites/tissues/organs and the action of drugs in these sites leads to intolerable side effects, poor drug delivery, and then emergence of resistance [4].

It aims to reduce systemic toxicity of drug and the emergence of resistance, while attaining unprecedented correctness in treatment. By using small molecules, photopharmacology provides a feasible alternative to optogenetics [5]. Whereas, serious indication of the different pharmacological targets in a broad range of organs and a study of organ systems in the human body that can be addressed in a non-invasive manner. The prospects for the target delivery of light to these organs and the exact necessities for light activatable drugs. It also aims to illustrate the drugability of medicinal targets with current findings and emphasize where conceptually new approaches have to be explored to offer photopharmacology with future prospects to bring "smart" molecular design eventually to the monarchy of clinical use [6].

The principle of photopharmacology consists in the introduction of molecular structure of bioactive compounds is a reversibly photoisomerizable drugs. Photoisomerizable drugs can be used to target localized diseases by light-activation of drugs exactly when and where they are required, leaving the rest of the treated organism unaffected, as schematically illustrated in

Figure-1 [6]. Localized activation might decrease the toxicity load imposed by the drugs on the patients. Furthermore, the drugs can be "turned off" by light next to the treatment to further decrease the side effect, toxicity and decreases resistance to develop during the treatment [7].



Photopharmacology are traditional pharmacology under control of light. Photocontrol can be either extrinsic (external light stimulus) or intrinsic (light from inside the body through *e.g.,* activation of fluorescence at the site of action). Critical factors are: Light-delivery, target-selection, choice of photoresponsive unit (photoswitch) and drug-optimization [8]. Other definitions may include the use of bio-compatible photo-removable drugs and usually light-responsive molecules. It is important, to mention that different approaches lead to various levels of control [9]. Photoswitches offer the advantage of switching between different states reversibly. Thus allowing for *e.g.,* locally activation and deactivation of drug. Also further temporal deactivation can be controlled by suitable choice of thermal stabilities of the active and inactive isomer. Furthermore, various modality selective action can be attained in special cases, whereas, the various isomers of the photoswitch show preferences for various pharmacological targets [10].

Azobenzenes -The photoswitches

Previous researches by observing for a molecule that had two mirror image versions - or isomers - which could be switched using light [11].

The isomers required to have different shapes, so the switch was likely to alter the conformation of any attached drug and therefore the drug has ability to reach its target site. In this way light could be used to switch drug activity on or off. The observable molecule was azobenzene ($C_{12}H_{10}N_2$), and is used extensively as a dye and food colourant. The molecule consists of two rings of benzene linked by a nitrogen - nitrogen double bond [12].

Azobenzenes, the little photoswitches that could' - very reliable little engines with which to drive things." The steadier *trans* isomer has the benzene rings on reverse sides but, on radioactivity with ultraviolet (UV) light, this switches to the *cis* verification, with the benzene rings sitting next to each other. In time, the molecule reverts to the steadier *transform.* Azobenzenes also advantage from being a large pre-existing list of toxicity data owing to their extensive industrial use [13].

Restoring Sight

The most advanced photopharmaceutical research and development is being carried out by Photoswitch Biosciences is developing a light-responding drug that can regain sight.

Principal cause of blindness is degeneration of photoreceptor cells in the developed world and is extremely irreversible. Actually there is a degenerative condition such as age-related macular degeneration (AMD), genetic diseases, such as retinitis pigmentosa [14]. The light-sensitive receptor proteins which present

in the eye is called as opsins, are mainly in-built photoswitches. Which are present in membranes of retinal neurons, they work together with the light-sensitive vitamin A-based molecule retinal. A photon of light results in the photoisomerisation of retinal, which causes a conformational change in the opsin protein. This leads to a cascade of signaling by cell that leads to an electrical signal being sent to the brain [15].

Recently discovered that try to replace the opsins function by using a switchable drug containing a azobenzene molecule. The idea was to find a molecule that could directly block membranes of retinal cells through potassium ion channels, set off a signaling cascade similar to that created when photoreceptor proteins are working [16].

Chemotherapy side effects

Combretastatin A-4 (CA4) is a novel synthesis of a photoswitchable chemotherapy drug. The molecule has the capability to stop cell division by inhibiting the microtubules production of rigid, hollow rods of tubulin polymers that composition of a cell's cytoskeleton [17].

Drugs that inhibit the production of microtubules make up a major class of chemotherapies but, as with various anticancer drugs, their potent effects lead to severe side effects, which may limit dosages [18].

Photopharmacology may offer a new solution. "A new class of drugs that only hits microtubules". The novel CA4 molecule has a trimethoxybenzene ring, giving *cis* and *trans* isomers of the drug. The *cis* isomer is highly effective than the *trans* isomer. By substituting a carbon double bond with a nitrogen double bond and adding some extra functional groups, a new conventional compounds that named photostatins, whose drug action can be organized by blue light. The light causes a switch to the *cis* conformation, which is 250 times more toxic to cancer cells than the *trans* isomer. This method could be a novel treatment for skin cancers [19].

Diabetes and Beyond

Type 2 Diabetes Mellitus is commonly treated with drugs such as sulfonylurea, which stimulates insulin secretion by binding to its receptors present on pancreatic beta-cells. But therapy comes with some serious side effects, such as blood glucose decreases and increases in cardiovascular disease. Drug release control to the pancreas might avoid these actions by restricting the drug's actions to where it's needed, therefore reducing off-target physiological effects [20].

A novel drug Glimethoride is a third generation sulfonylurea, consist of an azobenzene unit. The drug activated after a meal, most probable using an implanted blue LED: "The drug switches on very rapidly in milliseconds, and because it switches off within about two seconds and able to get quite fine control [21].

Photopharmacology could also be used to target antibiotic resistance. It has been novel research in the field, has decades of knowledge in designing molecular switches for nanoelectronics and saw a prospect to try some of that experience to the problem of antibiotic resistance [22].

If antibiotic activity could be switched off outside the human body, this would help to prevent developing a resistance. Recently, it has designed several switchable versions of a quinolone antibiotic containing an azobenzene unit. These could be 'switched on' to their target site with UV light but 'switched off' automatically within hours [23].

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