Management of Treatment and Prevention of Acute OP Pesticide Poisoning by Medical Informatics, Telemedicine and Nanomedicine

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Abstract: *Acute organophosphorous pesticide (OP) poisoning kills a lot of people each year. Treatment of acute OP poisoning is of very difficult task and is a time taking event. Present day informatics methods (telemedicine), bioinformatics methods (data mining, molecular modeling, docking, cheminformatics), and nanotechnology (nanomedicine) should be applied in combination or separately to combat the rise of death rate due to OP poisoning. Use of informatics method such as Java enabled camera mobiles will enable us early detection of insecticidal poisoning. Even the patients who are severely intoxicated (suicidal attempts) can be diagnosed early. Telemedicine can take care for early diagnosis and early treatment. Simultaneously efforts must be taken with regard to nanotechnology to find lesser toxic compounds (use less dose of nanoparticle mediated compounds: nano-malathion) as insecticides and find better efficacy of lesser dose of compounds for treatment (nano-atropine) of OP poisoning. Nano-apitropine (atropine oxide) may be a better choice for OP poisoning treatment as the anticholinergic agent; apitropine and hyoscyamine have exhibited higher binding affinity than atropine sulfate. Synthesis of insecticides (malathion) with an antidote (atropine, apitropine) in nanoscale range will prevent the lethal effect of insecticides.*

Keywords: *OP poisoning, Molecular modeling, Docking, Nanomedicine, Telemedicine, Hyoscyamine, Apitropine.*

Introduction

With the advent of OP compounds as a chemical warfare neurotoxin agent in 1930's it is now the most widely used insecticide since it has very low environmental stability and a high effectiveness against different insect species [1]. They degrade rapidly by hydrolysis on exposure to sunlight, air and soil hence having insignificant ecological impact but are classified as "extremely hazardous" to human beings according to WHO. They are widely used in agriculture and public health pest control programs such as mosquito eradication [2].
These insecticides target the enzyme acetylcholinesterase which is required for normal control of nerve impulse transmission from nerve fibers to smooth and skeletal muscle cells as well as within the central nervous system. However, in some parts of the developing world, there is a general threat of easy availability of such insecticides due to poor regulation causing an excess use leading to poisoning and suicidal attempts. The human beings may become susceptible to the effects of organophosphates through accidental inhalation or ingestion through contaminated food sources. Since the organophosphates target acetylcholinesterase enzyme in insects, it is of major concern as it also induces toxicity in mammalian as the neurotransmitter acetylcholine is affected in human beings. The acute toxicity is due to irreversible inhibition of acetylcholinesterase from covalent interaction with the organophosphates leading to a synaptic accumulation of acetylcholine that ultimately effects into blockade of cholinergic synaptic transmission [1]. The enzyme acetylcholinesterase is critical to nerve function in human beings and even at very low concentration the organophosphates may be most hazardous to brain development of fetuses and young children [3].

The mainstay of OP poisoning is atropine sulfate administered intravenously or intramuscularly which diminishes the peripheral muscarinic manifestations of acetylcholine. It is a life-saving agent in organophosphate poisoning and depending on the severity of poisoning, doses of atropine ranging from very low to as high as 300 mg per day may be required [4].

Aging is a phenomenon occurring with organophosphate and enzyme complex that physiologically needs a long period for synthesis of new acetylcholinesterase to detoxify the organophosphates. The treatment regimes for the poisoning additionally consist of oxime like pralidoxime which reactivates the phosphorylated enzyme. They act as reversible inhibitors competing with organophosphates preventing aging leading to slow restoration of normal enzymatic activity as the insecticide dissociates from the enzyme. They are effective in treating moderate or severe poisoning. However, they should be given as soon as possible before aging takes place, are not broad-spectrum antidote since they are not active against all the organophosphate insecticides and other limitations being the cost, stability and availability of the oximes [1].

The basic clinical diagnosis of organophosphate poisoning is based on the depression in level of serum cholinesterase and red blood cell cholinesterase although there is a small proportion of population having a genetically low level of plasma cholinesterase. In some patients lowered plasma cholinesterase may be due to other pathophysiological conditions or exposure to other toxicants. However in remote areas there is lack of such sensitive detecting facilities to predict the outbreak of such poisoning due to environmental or food contamination with the insecticides. Such remote area requires a monitoring unit to detect and quantify the level of insecticide present in any natural transmitting form like water, air or food.

Insecticides are pervasive and potent chemicals which can be problematic in the environment even at low concentrations. Methyl parathion is an insecticide widely used for the control of sucking and chewing insects. While there are a number of methods for its detection in samples such as soil, groundwater and food, a compromise must be reached between sensitivity, selectivity, cost and ease of use. Methyl parathion is an insecticide and acaricide used to control boll weevils and many biting or sucking insect pests of agricultural crops. It kills insects by contact, stomach and respiratory action. Methyl parathion is available in dust, emulsifiable concentrate, Ultra-Low-Volume liquid, microencapsules and wettable powder formulations [5]. Methyl parathion is one of a class of insecticides referred to as organophosphates. These chemicals act by interfering with the activities of cholinesterase, an enzyme that is essential for the proper functioning of the nervous systems of humans, animals and insects. As a pesticide, parathion is generally applied by spraying. It is often applied to rice, cotton, spinach and food trees. The usual concentrations of ready-to-use solutions are 0.05 to 0.1%. Methyl parathion is highly toxic by inhalation and ingestion, and moderately toxic by dermal adsorption. As with all organophosphates, methyl parathion is readily absorbed through the skin. Skin which has come in contact with this material should be washed immediately with soap and water and all contaminated clothing should be removed. Accidental inhalation and skin exposure to methyl parathion have caused human fatalities. Methyl parathion may cause contact burns to the skin or eye [6]. The organophosphate insecticides are cholinesterase inhibitors. They are highly toxic by all routes of exposure. When inhaled, the first effects are usually on respiration and may include bloody or runny nose, coughing, chest discomfort, difficult or short breath, and wheezing due to constriction or excess fluid in the bronchial tubes. Skin contact with organophosphates may cause localized sweating and involuntary muscle contractions. Eye contact will cause pain, bleeding, tears, pupil constriction, and blurred vision. Following exposure by any route, other systemic effects may begin within a few minutes or be delayed for up to 12 hours. These may include pallor, nausea, vomiting, diarrhea, abdominal cramps, headache, dizziness, eye pain, blurred vision, constriction or dilation of the eye pupils, tears, salivation, sweating, and confusion. Severe poisoning will affect the central nervous system, producing incoordination, slurred speech, loss of reflexes, weakness, fatigue, involuntary muscle contractions, twitching, tremors of the tongue or eyelids, and eventually paralysis of the body extremities and the respiratory muscles. In severe cases there may also be involuntary defecation or urination, psychosis, irregular heartbeats, unconsciousness, convulsions and coma. Death may be caused by respiratory failure or cardiac arrest [7]. It generally disrupts the nervous system by inhibiting the acetylcholinesterase. It is absorbed via skin, mucous membranes, and orally. Absorbed parathion is rapidly metabolized to paraoxon, as described above. Paraoxon exposure can result in headaches, convulsions, poor vision, vomiting, abdominal pain, severe diarrhea, unconsciousness, tremor, dyspnea, and finally lung-edema as well as respiratory arrest. Symptoms of poisoning are known to last for extended periods of time, sometimes months. The most common and very specific antidote is atropine in doses of up to 100 mg daily [3].

Recently tragedy come during January month 2012 were four members died from one family (9 yrs Male; 16 yrs Male; 11 yrs Female and 78 yrs Female) and 2 members from another nearby family (80 yrs Male and 14 yrs Female) in Munger district of Bihar (India) due to toxicity of insecticide. All these deaths were due to OP poisoning and now it is high time for us to rethink over how to treat and manages.

Advances in detection and identification of OP poisoning

Different methods have been applied for the treatment or prevention of acute organophosphate pesticide poisoning. To find novel drug candidates we are describing here various methods below. One method follows bioinformatics based molecular modeling and docking studies for finding novel compounds by using different drug designing programs and softwares which are described below. Other informatics method like telemedicine utilizes telephonic technology for immediate treatment of OP poisoning. Another method i.e. nanotechnology or nanomedicine utilizes protocols which can lessen the toxicity of drug or pesticide in the individual.

Comparative modeling, simulation and docking studies

The crystal structure of human acetylcholinesterase (AChE), a complex with methylene blue (PDB ID: 2W9I) responsible for OP toxicity was obtained from the Protein Data Bank (PDB) [8, 9]. The ligand molecules of the crystal structure of AChE protein were removed. The water molecules were removed from the surface of the protein. The extra water molecules will mask the protein surface from the ligand. All protein 3D models were prepared for docking by removing water and hetero atoms for docking analysis by Discovery Studio (DS) v2.5 software. The different atropine analogues were downloaded from the Pubchem compound search at National Center of Biotechnology Information (NCBI) database.

The force field was applied to the crystal structure of acetylcholinesterase (PDB id: 2W9I) by CHARMM (Chemistry at HARvard Molecular Mechanics) in DS v2.5, in which powerful mechanics and dynamics protocols were used for studying the energetic and motion of molecules. Molecular dynamics simulations were carried out using the CHARMM module in standard dynamics cascade protocol in DS v2.5. The protein atoms were parameterized using the CHARMM force field. All bond lengths involving hydrogen atoms were fixed using SHAKE algorithm [10]. Simulations were carried out at 300 K with 2000 steps of steepest descent minimization techniques, minimization root-mean square (RMS) Gradient (0.1), minimization energy change (0.0), implicit solvent model (distance-dependent dielectrics) until the root-mean square deviation (RMSD) was less than $0.001 \cdot kcal \cdot mol^{-1} \cdot Å^{-1}$.

The binding sites were predicted by MetaPocket server [11]. MetaPocket follows a consensus method in which the predicted sites from four methods: LIGSITE, PASS, Q-SiteFinder, and SURFNET are combined together to improve the prediction success rate. The potential 5 ligand binding sites were generated using a probe of radius 5.0 Å. The binding site having highest z-score was selected for further investigation [11]. The binding sites were also predicted by binding site module of DS v2.5. The binding site module is a suite of DS for identifying and characterizing protein binding sites and functional residues in proteins. The entire amino acid sequence of acetylcholinesterase was selected, and a CHARMM force field was applied for the preparation of the protein. The binding sites of the model were compared with the binding sites of template as well as the binding site predicted by MetaPocket server. The binding sites and the functional residues were identified and stored for further investigation.

The DS package was used to dock approximately 80 analogs of atropine onto our crystal structure of acetylcholinesterase. A local virtual compound library of the analogs was designed. For ligand protein interaction, the ligands were optimized using the Prepare Ligands tool of DS v2.5. The optimized molecules were docked into our refined model using "LigandFit" [12] and Genetic Optimisation for Ligand Docking (GOLD) v4.1 [13]. The binding affinity of each compound is estimated from different scoring schemes

(DS v2.5) like Dock score in LigandFit module of DS by choosing the consensus score. For each ligand, 10 poses were generated and scored using scoring functions.

Mathematical formula for LigandFit score (DS v2.5):

Dock score (*force field*) = − (*ligand*/*receptor interaction energy* + *ligand internal energy*).

There are two energy terms in the force field version of Dock score, internal energy of the ligand and the interaction energy of the ligand with the receptor. The interaction energy is taken as the sum of the van der Waals energy and electrostatic energy. The computation of the interaction energy can be quite time consuming. To reduce the time needed for this calculation, a grid-based estimation of the ligand/receptor interaction energy is employed. The van der Waals component of the force field interaction energy typically exhibits a steep rise at short interatomic distances, which can have undesirable consequences in the context of ligand-receptor docking. In particular, the combination of approximating the receptor structure as rigid and limited sampling of ligand conformational space tends to overly penalize poses with "mild" short contacts between the ligand and receptor, due to the "hard" nature of the van der Waals potential as defined in most standard force fields. To overcome this tendency, a softened form of the van der Waals potential is employed with the DockScore function. This softened potential rises to a large but finite value at zero interatomic separation. To maintain a proper balance between electrostatics and van der Waals, the electrostatic energy is also softened to prevent it from dominating the van der Waals energy at short separations. The internal energy of the ligand is computed when using the force field version of Dock score. The purpose of including the internal energy is to avoid ligand conformations with bad internal nonbond clashes. By default, only the standard (not softened) van der Waals energy is used for the ligand internal energy. Including electrostatic energy as part of the ligand internal energy is optionally available [14].

Docking experiments of different analogues of atropine with acetylcholinesterase structure were also performed in GOLD v4.1 software using the default GOLD fitness function (VDW = 4.0, H-bonding = 2.5) and evolutionary parameters: population size = 100; selection pressure = 1.1; operations = 100,000; islands = 5; niche size = 2; migration = 10; mutation = 95; crossover = 95 [14]. Scoring function "Goldscore" was used for evaluation of different docking.

Mathematical formula for GOLD Docking

$$Fitness = S(hb\_ext) + 1.3750S(vdw\_ext) + S(hb\_int) + 1.0000S(vdw\_int),$$

where $S(hb\_ext)$ is the protein-ligand hydrogen bond score, $S(vdw\_ext)$ is the protein-ligand van der Waals score, $S(hb\_int)$ is the score from intramolecular hydrogen bond in the ligand and $S(vdw\_int)$ is the score from intramolecular strain in the ligand.

Five docking runs were performed per structure. If at any time 3 of the 10 poses were within 1.5 Å RMSD of each other, the docking run for that structure was terminated and docking calculations began for the next structure. Best three poses and docking scores were outputted into a *.mol file and text file respectively. Among these poses, the most suitable docking mode with a high dock score and a high fitness score from consensus functions was finally selected. Docking of various important proteins with different molecules in both GOLD and DS has already been reported [15].

Telemedicine technology has evolved in India few years ago. Different telemedicine approaches have been followed to prevent or eradicate few vulnerable diseases throughout India i.e. point to point system, point to multipoint system, multipoint to multipoint system and teleeducation. Real time telemedicine can involve a single link between patient end and a single specialist or it can involve the single patient end and multiple specialist ends. First is called Point to Point System, second is called Point to Multipoint System. In Point to Point System – one patient end connects to one specialist doctor within the hospital. In Point to Multi Point System – one patient end at a time connects to any of the specialist doctors' end within the hospital. Multi Point to Multi Point System – several patients' end simultaneously connects to different Doctors' end at different hospitals at different geographical locations. Major areas of telemedicine technology involves teleconsultation, telediagnosis and teletreatment where the patient with the local doctor consults the specialist, obtains the line of treatment. Telemonitoring is a regular monitoring duty for intensive care and emergency care whereas Telesupport supports during disaster management. For real time telemedicine hardware setup includes a PC, communication link (Dial up, broadband internet or satellite link), and equipment for capturing patient data, like digital or video camera, printer/scanner, and also a videoconferencing system at the patient end. At the doctor end where the patient data is received, analyzed and opinion is given by expert also needs a PC, communication link (Dial up, broadband internet or satellite link), videoconferencing system.

Management of treatment and prevention of acute OP pesticide poisoning

OP compounds or organophosphates are absorbed into the body via the digestive tract, skin and mucus membranes; they are also absorbed through the respiratory tract if inhaled. The patient may have the typical smell of OP compounds, which is a pungent garlic-like odor. The patient may have slow heart rate and low blood pressure causing dizziness and fainting; rarely the patient may have a high blood pressure and fast heart rate. The heart rhythm may be abnormal and could cause death in severe cases. The patient may experience difficulty in breathing due to increased secretions and spasm of the bronchi (breathing may be maintained by inserting a tube into the trachea). Artificial ventilation may be needed in some cases. Pulse, blood pressure and heart rate and rhythm should be carefully monitored. The patient may need intravenous fluids to maintain the blood pressure. They may have an increase in salivary secretion, pain in abdomen and loose stools. He may also have incontinence of urine and stool. Vision may be blurred due to small pupil size and increased tear formation. Rarely the pupils may be larger than normal in size and sweating excessively. Muscles may be affected leading to twitches, cramps, muscle weakness and eventually muscle paralysis. Death could occur if the diaphragm and other respiratory muscles are affected. Brain may be affected leading to anxiety, confusion, memory loss, irritability, seizures or coma. Death could occur due the above symptoms such as abnormal heart rhythm, difficulty breathing, and paralysis of respiratory muscles or coma.

A review for management of the treatment of acute OP pesticide poisoning [16] by Michael Eddleston and colleagues recommended pralidoxime chloride or obidoxime as a loading dose followed by an infusion until atropine has not been needed for 12-24 hr as well as pretreatment with the oxime in case of recurring cholinergic features. This recommendation is not evidence based and should not be regarded as the gold standard. Eddleston and colleagues present many theoretical and practical reasons why oximes might not be useful to patients with overwhelming self-poisoning, but they do not translate these considerations into clinical practice. A placebo-controlled trial of oxime treatment for OP pesticide poisoning showed that pralidoxime plus atropine does not have any benefit over atropine alone [17].

Treatment of such poisoning must be done immediately after poisoning but in remote villages in India only insecticides are given. As per reviews class I pesticides should be banned, which is not done in Asian countries till date [18]. John Victor Peter and colleagues told that replacing highly toxic OP insecticides with less toxic insecticides will substantially reduce deaths from pesticide poisoning. One can agree that other public-health measures, particularly reducing the concentration of pesticide in available preparations, could have major effects. But there is no shortcut method available for immediate detection of pesticide poisoning. To prevent this type of poisonings, we can afford different techniques presently available throughout the world. High throughput screening can be imagined for finding novel compounds against acetylcholinesterase protein by molecular modeling and docking methods (virtual screening). Even telemedicine technology can be utilized for early detection. Nanotechnology can also be followed for better insecticidal properties at lower dose of OP pesticide and have lesser toxicity in human.

Virtual screening of compounds

Docking represents the mathematical calculation of the most probable spatial orientation between two interacting molecules, usually a protein and a small ligand, two interacting proteins, or DNA and protein. Various parameters are calculated to evaluate possibility of such interaction. For molecular docking we used DS v2.5 software. We accessed the tertiary structures of human proteins like acetylcholinesterase from PDB with the proposed interaction with atropine analogues and are summarized in Fig. 1 and Table 1. There were sixteen different active sites of protein that were defined from the volume of ligand method available in the binding site module. The sphere was defined over the binding site with a radius of 5 Å from the centre of the binding site. Fig. 1 shows the highest dock score of AChE protein of human interacts with different atropine analogoues in which atropine oxide (apitropin) shows the highest interaction with target protein (97.91) and shows the highest number of 20 H-bond (in all ten poses) present in lowest interaction with difenoxin (45.393) but it shows the second highest number 15 H-bond.

Ten different binding conformations of various ligands with the AChE enzyme crystal structure, which were ranked with LigandFit score, were also detected during the study. For more than eighty compounds, docking run was performed by ligandfit protocol of DS v2.5 to predict ligand protein interactions of various ligands and found that atropine oxide showed the highest dock score as summarized in Table 1. The amino acids (Asp72, Tyr121, Tyr334 and His440) of AChE are frequently involved in forming hydrogen bonds (20), which signify that atropine oxide is the best drug and shows the suitable interaction with AChE protein are shown in Fig. 2 (A). All other atropine analogues have also shown the best interactions with target protein like dock score of hyoscyamine (63.708: 12 H-bonds; Tyr121, Tyr334 and Asp72), atropine (58.753: 6 H-bonds: Asp72, Tyr121) are shown in Fig. 2 (B) and cystospaz (58.426: 5 H-bonds; Asp72, Tyr121). The Piecewise Linear Potential1 (PLP1) and PLP2 [19, 20] are the energy function for docking that specified for atropine oxide as 79.14 and 77.94 respectively. The Potential of Mean Force (PMF) is a statistical analysis approach using 3D structure databases to provide a fast and accurate prediction of protein-ligand binding free energies gave a score of 145.36 with atopine oxide [21]. We have already reported interaction to different proteins and ligands [22, 23, 24].

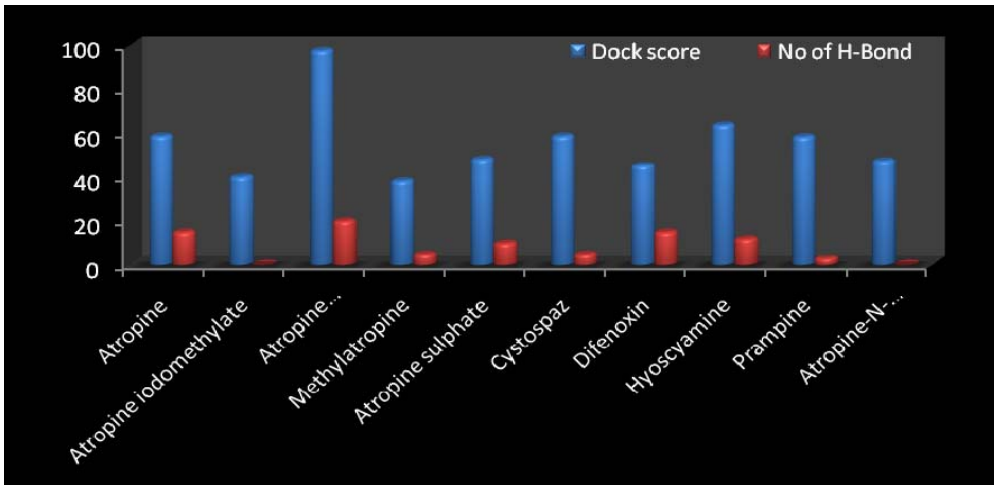

Fig. 1 Graph showing docking scores and number of H-bonds of different atropine analogoues

Table 1. The list of compounds which have exhibited better binding affinity with acetyl cholinesterase enzyme by virtual screening

Ligands	**Dock score**	**Residues involved in H-bond**
1. Atropine	Site1: 10 pose 58.753: 15 H-bonds Site5: 10 pose 43.568: No H-bonds	Asp72, Tyr121
2. Atropine iodomethylate	Site5: 10 pose 40.138: No H-bonds	No H-bonds
3. Atropine oxide (Apitropin)	Site1: 10 pose 97.91: 20 H-bonds Site2: 10 pose 42.9: 10 H-bonds Site4: 10 pose 53.637: No H-bond Site5: 10 pose 74.672: 15 H-bonds	Tyr121, Tyr334, Asp72, His440 Tyr121, Tyr458 No H-bond Tyr458, Met83
4. Methylatropine	Site5: 10 pose 38.345: 5 H-bonds	Tyr121
5. Atropine sulphate	Site1: 10 pose 48.345: 10 H-bonds	Tyr121, Tyr458
6. Cystospaz	Site1: 10 pose 58.426: 5 H-bonds	Asp72, Tyr121
7. Difenoxin	Site5: 10 pose 45.393: 15 H-bonds	Tyr121
8. Hyoscyamine	Site4: 10 pose 63.708: 12 H-bonds	Tyr121, Tyr334, Asp72
9. Prampine	Site1: 10 pose 58.411: 3 H-bonds	Tyr121
10. Atropine-N-octylbromide	Site1: 10 pose 47.536: No H-bonds	No H-bonds

Telemedicine and information technologies based prevention of OP poisoning

Telemedicine or telemedicoinformatics is an approach for safe, economic and rapid diagnostic and treatment of patients. Telemedicine is the use of Information and Communications Technologies in order to provide healthcare practitioner at a distance. Telemedicoinformatics is the conversion of data into knowledge through information which provides the meaningful result. The term used only to care a patient record and on the basis of previous data we have to decide other patients quickly which results in safe, economic and rapid diagnoses of the patient. Telemedicine helps to eliminate the distance barriers and can improve access to medical services that would often not be consistently available in distant rural communities. It

is also used to save lives in critical care and emergency situations. Although there were distant precursors to telemedicine, it is essentially a product of 20th century telecommunication and information technologies (IT). There are a number of tragedies occurring in remote rural areas every year where even the physicians are unable to come to treat the patients immediately, hospitals are miles away from the site of poisoning. The death of distant rural people due to OP insecticidal poisoning in Munger district (Bihar) could have been prevented by telemedicine technology. The death was due to the consumption of leafy vegetables which were recently sprayed with OP insecticides. The leafy vegetables must have been washed thrice before using them for culinary purposes. Telemedicine helps the patients for easy early diagnosis and treat the patients who are in the remote areas. These technologies permit communications between patients and medical staffs with both convenience and fidelity, as well as the transmission of medical, imaging and heath informatics data from one site to another. Early forms of telemedicine achieved with telephone and radio have been supplemented with video-telephony, advanced diagnostic methods supported by distributed client/server applications, and additionally with telemedical devices to support in home care [25].

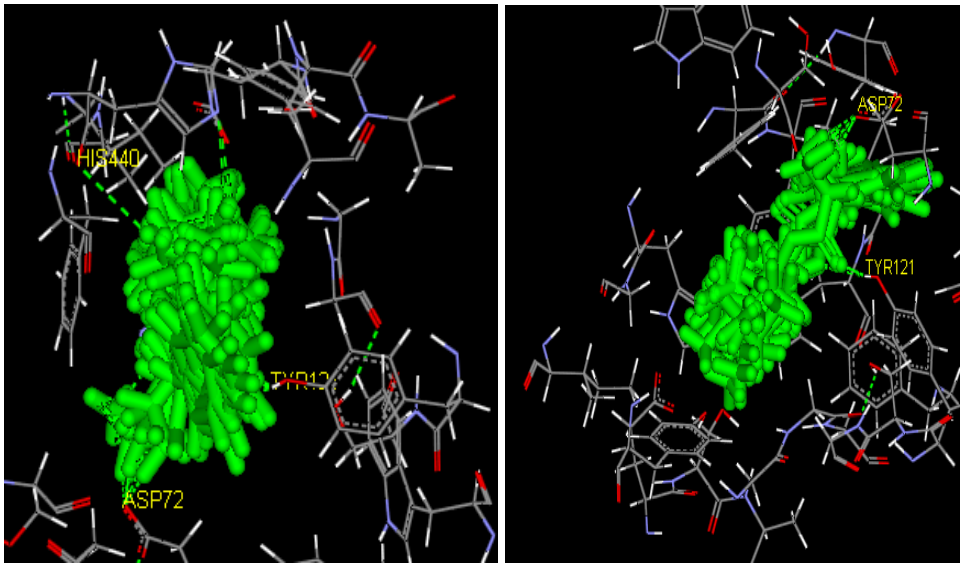

Fig. 2 Protein-ligand an interaction shown represents of atropine oxide (A) and atropine (B) with ACHE protein (2W9I) of ten different conformations (poses).

Providing healthcare to India's over one billion population of which about 75% live in villages, is a formidable task. About 75% of the doctors practice in urban areas and 23% in semi-urban areas. This leaves just 2% of the qualified doctors, who are attached to about 23,000 primary health and 3000 community health centers, to attend to 70% of the population living in villages. ISRO's telemedicine pilot project was started in the year 2001 with the aim of introducing the telemedicine facility to the grass root level population as a part of proof of concept technology demonstration. The telemedicine facility connects the remote District Hospitals/Health Centers with Super Specialty Hospitals in cities, through the INSAT Satellites for providing expert consultation to the needy and underserved population [26]. Current status of the standardization effort in India is the management of disease with an expanding application of telemedicine [27]. Entities involved in telemedicine are telemedicine platform (Desktop PC, Laptop), telemedicine software, clinical devices (digital ECG, electronic stethoscope, and high resolution camera) and Communication Media etc. that are shown in Fig. 3.

The widespread adoption of telemedicine is a major and still underdeveloped challenge that needs to be strengthened through new research directions includes four hypotheses, which are all susceptible to experimental verification. In particular, the data about the adoption of telemedicine should be collected from applications implemented on a large-scale, to test the assumption that the adoption of telemedicine follows an S-shaped growth curve. This will lead to a better understanding of the process, which will in turn accelerate the adoption of new telemedicine applications in future [28]. Research is also required to identify suitable financial and professional incentives for potential telemedicine users and understand their importance for widespread adoption.

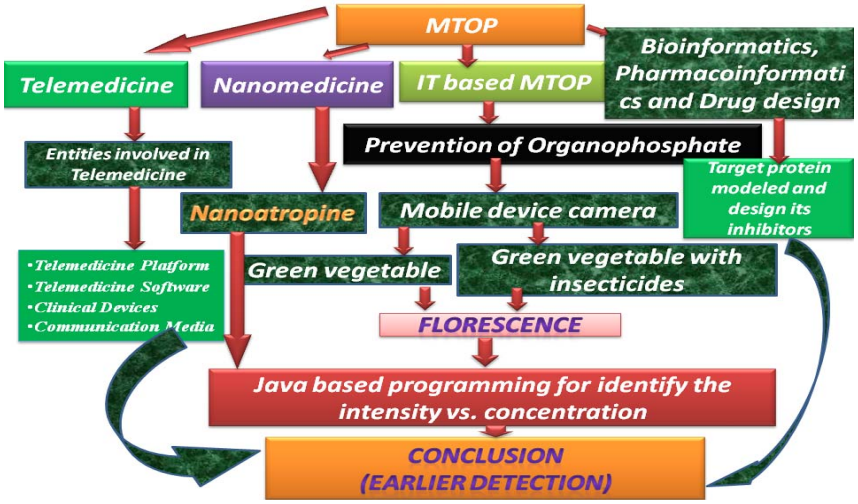

Fig. 3 Flow chart representing a process for management of treatment of acute OP poisoning (MTOP). The flowchart represents four typical procedures for the management of treatment of patient suffering from acute organophosphate poisoning i.e. telemedicine, nanomedicine, bioinformatics related to drug design (virtual screening) and information technologies based management of organophosphate poisoning (IT based TOP).

Prevention of acute organophosphate poisoning by IT

The implementation of IT and communication technology for prevention of acute organophosphate poisoning by using the Java enabled mobile camera based on distinction of fluorescence between fresh vegetable and insecticide treated vegetables by florescent detection methods. The ideal fluorescent intensity of green vegetable is compared against green vegetable with treated organophosphate compound and the intensity difference found is directly proportional to concentration of particular poison.

In spectroscopy, the absorbance A (also called optical density) [29-31] is defined as:

$$A\lambda = \log_{10} (I_0/I),$$

where I is the intensity of light at a specified wavelength λ that has passed through a sample (transmitted light intensity) and I_0 is the intensity of the light before it enters the sample or incident light intensity (or power). Absorbance measurements are often carried out in analytical chemistry, since the absorbance of a sample is proportional to the thickness of the sample and the concentration of the absorbing species in the sample, in contrast to the transmittance I/I_0 of a sample, which varies exponentially with thickness and concentration.

Absorptance [32] (not absorbance) is defined as: the ratio of the radiant flux absorbed by a body to that incident upon it. It is also called [absorption] factor. Total absorptance refers to absorptance measured over all wavelengths. Spectral absorptance refers to absorptance measured at a specified wavelength. Absorbance spectra are typically used to define photo-pigment spectra because their shape, when normalized (i.e., plotted as a fraction of the maximum absorbance), is independent of pigment optical density (pigment concentration). In contrast, the absorptance spectrum, like the spectral sensitivity of the human subject, broadens as the optical density increases [33]. Outside the field of analytical chemistry, e.g. when used with the Tunable Diode Laser Absorption Spectroscopy technique, the absorbance is often defined using the natural logarithm instead of the common logarithm, i.e. as

$A\lambda = \ln (I_0/I)$.

Nanoinsecticides: a novel approach to reduce toxicity of insecticides in human beings

Nanotechnology is significant on account of its pre-eminence upon the comprehension, use, and control of matter at magnitudes of a minute scale, akin to approaching atomic levels, with which to manufacture new substances, instruments, and frameworks. It is also known as "Molecular Manufacturing", it is an emergent diversity of technologies in which medicine and engineering come together with physics and chemical science which are opening up many brand new possibilities especially within the medical arena in terms of implantable transmission methods, which are often favored to the application of injectable medicine. One, if not the most important, aspects of the applications of nanotechnology is the incorporation of this science into medical programs embracing the present research into vaccine formation, toxic control, wound regeneration, skin care, narcotic countermeasures and chemical and biologic detectors. The biological in addition to medicinal study areas, have utilized the unequalled properties of nanomaterials for various programs not least due to their aspiring enhanced delivery methods, such as pulmonic or epidermic systems to prevent having to pass throughout the abdomen but it can be used as reduced form of insecticides in agriculture. For the control of size, shape and composition of these insecticides, we can synthesize nano-insecticides (insecticide in nanoparticle form) that spray or use in agriculture field and this can be remedy for insecticide toxicity in human beings. Nanoscale insecticides will not only increase the efficacy and potency of these insecticides but also it will be useful in decreasing the dose of insecticides that are used in agriculture, for example methyl parathion the usual concentrations of ready-to-use solutions are 0.05 to 0.1% [7], nanoinsecticides will be able to reduce dose or concentration by the surface modification of methyl parathion, conjugate with biocompatible nanoparticles and synthesize by chemical or physical method [34]. Another option is also to synthesize these insecticides with an antidote (e.g. atropine) in nanoscale range to prevent the lethal effect of these insecticides that also help in increasing the potency and efficacy of atropine with less than the available dose and in the mean time it reduces the toxic effect on human body. Nanoinsecticides will be a noble weapon to stop the killing of a person due to toxic effects of insecticides.

Concluding remarks

Recently sudden death of six people of different age groups including female children belonging to two separate families in Munger district of Bihar (India) due to OP poisoning is of national concern. The four advanced technologies can be integrated to virtually decline the rate of death due to sudden OP poisoning in remote rural areas. Ideally telemedicine and IT based management of treatment of organophosphate poisoning may be precisely utilized for early detection of poisoning. Mobile camera based on Java technology will be valuable in

early detection of OP compounds to prevent poisoning. Other two advanced technologies nanomedicine and bioinformatics related to drug design (virtual screening) may be precisely utilized to obtain novel compounds as insecticides but will have lesser toxicity than the presently available insecticides. In virtual screening among different anticholinergic agents, apitropine (atropine oxide) has exhibited higher binding affinity with acetylcholinesterase than that of atropine sulfate, which is presently used as antidote of OP pesticide poisoning. Even hyoscyamine has exhibited better binding affinity than atropine sulfate. Even these two technologies (nano-atropine or better compound than atropine i.e. nano-apitropine (atropine oxide)) may be applied to find better therapy against pesticide poisoning. Efforts should be carried out to find novel insecticidal compounds (based on nanotechnology and bioinformatics) which are having lesser toxicity to human beings than presently available pesticides e.g. malathion. Even mobile telemedicine facility can also be considered for the prevention of death due to OP poisoning [35].

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