New Horizon in Drug Development

* Hina Masood** Mohammad Tariq Aftab

Abstract:-

Unraveling the complexity of human structure and the function has been the focus of effects of pharmacologists & Scientists since long. They are exploring areas in drug development. This article reviews the possible future drugs in the field of memory enhancement and Gene therapy. Memory enhancement can be appreciated but pain of recalling of past set backs are unavoidable.

Introduction:-

By disclosing the laws of nature, Pharmacologists are always in search of different disease modalities and drugs are not only used in the treatment & diagnosis of a disease but also in their prevention. Neuroscience is an exciting field of Drug Development. Knowledge of neurotransmission and control mechanism may render the development of potential drugs. Among these, hidden memory and cognition facilitators and potential gene therapy are prominent.

Sources and selection Criteria:--

We selected articles of interest from 1999 and onwards, focusing on, memory enhancing drugs and anticancer therapy by using Gene therapy.

Future Memory Enhancing Therapies:--

Psychologists improve memory by “PQRST” method which stands for Preview, Question, Read, Self recitation, and Test (5), but ‘Memory’ can be enhanced with more powerful drugs in near future. To support this statement, I would like to share Kandel’s research (a noble prize holder) published on March 09, 2001 in huge Howard Medical Institute (HHMI), who genetically engineered mice with enhanced memory. (1) Eric R. Kandel created a mice by inserting a gene that when activated by the antibiotic, Doxycycline, produces the effect of other enzyme PKA in signaling pathways (PKA is a Kinase, which adds a phosphate to enzyme and Calcineurin is a phosphatase, which removes a phosphate) generating a long term potentiation (LTP). (1) LTP enhances connection between neurons and is one of the neural pathways by which memories are stored in the brain. He researched that by inhibiting the action of Calcineurin, he would enhance long term potentiation and memory storage. The researchers then measured the animals’ memories in behavioral test and found that Calcicain inhibited animals were better able to remember when familiar objects were moved to novel actions. These drugs do not effect other parameters like they can see, smell, locomote perfectly well & are motivated and by switching off the Calcineurin Inhibition, memory enhancement can be reversed.

Another scientist Gary Lynch searched a mechanism based memory enhancement drug Ampakines, first allosteric modulators transmission, which acts on brain by slowing down desensitization deactivation. (2) He searched that AMPA type glutamate receptors generate depolarization needed to unblock voltage sensitive NMDA type glutamate receptors which admit calcium in to dendrites. These AMPA type glutamate receptors would improved delayed recall in aged human. Repetitive release of transmitter allows AMPA receptors to generate sufficient depolarization to Unblock NMDA receptors and thereby induce LTP. Increasing the amount of glutamate releasable, during stimulation or enhancing the effects of the transmitter on AMPA receptors can reduce this requirement. So, if we develop such drugs which can stimulate AMPA receptors, we would be able to facilitate our memory.

Most researchers are now of the opinion that enhanced post synaptic current that define LTP expression i.e. long term potentiation of memory, are caused by changes in AMPA receptors. He also searched that simply adding new receptors to the synapses would increase the response to a given amount of transmitter which means recycling is co-opted so as to alter receptor numbers or their extent is modified to enhance their operation. His searches globalizes with assumption that steps in memory formation corresponds to steps in synaptic modification and drugs that enhance initial coding and later consolidation of memory, all expected to promote their behavioral reflection.

To, demonstrate this, he used different species like monkey, mice & rabbits, and in all these animals positive modulation of AMPA receptors decreases the requirement for their encoding of memory and it improves objects’s recognition without affecting their motor performance (28th Oct---

* Lecturer Pharmacology, Baqai Medical College, Baqai Medical University.
** Professor of Pharmacology, Baqai Medical College, Baqai Medical University.
Other cognitive enhancers, such as Cholineseresterase inhibitors like Metrifinase, Rivastigmine & Galantamethine are under process. (6) Nevertheless, few drugs have so far shown to improve consistently & substantially, impaired or normal memory in human over longer periods but their side effects can not be ignored in utilizing these drugs in future.

**An Approach to potential Gene Therapy:**

This is another potential area, which I want to focus. Until now disease only has disastrous effects but as the coin has two sides one is different from the other, in the same way, one disease can be beneficial for other diseases. The idea that virus can kill other cells has been captured by Dr. Russell of Mayo Foundation for medical education & research, a Ph D scientist (3). He demonstrated that as liver cells can be killed by Hepatitis virus or polio virus can kill nerve cells; Measles virus can kill ovarian cancer cells without harming the patient. The measles virus was first isolated from throat washing of a measles patient & was attenuated by growing cells. As cells are inoculated in few culture dish, cell mutation takes place. Dr. Russell discovered that these viruses can destroy cancer cells where it protects them against the damaging effect of natural host defense protein.

Measles virus has been tested against a variety of tumors in animal models where it shows a broad spectrum of activity against Lymphoma, Gliomas and Pancreatic cancer. (3)

Dr. Peng and her colleagues first grew ovarian cancer cells in the peritoneal cavity of mice. When they administered a measles expressing the soluble marker into the peritoneal cavity to treat these tumors, mice, that has got control (non active) virus died, while mice who received the therapeutic virus lived much longer than the control treated animals. (3)

So, this necessitate the development of viral vector production and this leads to the development of clinical protocol for approval of new drug by (IND.) Food and Drug administration Investigational New Drug. This will bring the new era in genetically engineered drugs.

Engineers have developed technology for targeting the virus to specific sites in the body by displaying monoclonal antibodies on viral coat, and they have inserted additional genes that make it easier to monitor viral spread and elimination in treated patient. They have treated both unmodified and genetically engineered virus. **Conclusion:**

This gives us the clue that understanding of a mechanism and exploration of Patho-physiological process of diseases and their application will lead to new areas on which drugs can be developed and Pharmacologists will have the better control on disease therapies. These drugs, and a large numbers of other drugs on different subjects and systems, can be proposed to have potential for future trend in drug development. This paper is too short to describe them but it can create a gate way of thinking about better areas of drug modification. But during exploring these areas, their untowards effects can not be ignored.

**References:**