Chapter 7
Enzymatic Research Having Pharmaceutical Significance

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ABSTRACT

The enzymes' biocatalysts act by lowering the activation energy without getting consumed in the reaction. The immense number of enzymes acts as a correctly matched orchestra to ensure that enormously complex life mechanisms and processes occur in a right direction. Sufficient quantity and accurate function of enzymes results in proper functional maintenance of body. The enzymes play a major role in the diagnosis, curing, biochemical investigation, and monitoring of many dreaded diseases of the century. The development of recombinant DNA technology had a significant impression on production levels of enzymes. Around 50% of the enzyme market is covered by recombinant enzymes. Because of development in molecular biology tools, several pharmaceutically enzymes have been identified and are being actively used in the pharmaceutical industry either for diagnostic or treatment. Information on this topic is very insufficient, and thus, the present chapter is an attempt to compile information on the sources, properties and applications of important therapeutic enzymes.

INTRODUCTION

In a few decades back the life expectancy of humans has increased from 45 years to 77 years globally because of significant advances in the medicine and pharmacy (Kola & Landis, 2004). The pharmaceutical industry is one of the fastest growing industries globally producing substantial revenue around the world (Kola & Landis, 2004). For the growth and development of any pharmaceutical industry, it must create unique products. Recombinant or therapeutically necessary enzymes come under the class of exclusive products which generate high revenue for the manufacturer. Pharmaceutical companies usually

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invest money for very long time so to find essential factors for the diseases. Hence, the development of the novel drug targets and the lead compound is essential for humankind.

Drug targets can be of many kinds including receptors, transcription factors, growth regulators, cytokines, hormones, and enzymes. Enzymes are biocatalysts they catalyze most of the biological reactions by lowering the activation energy without interfering with initial and final energy states of the reaction. They are most significant drug targets as they play an essential role in metabolic pathways which are the culprit of the metabolic anomalies like cancer and neurodegenerative diseases and metabolic disorders.

There are so many enzymes that play a part in the cancer GTPases are a group of enzymes that play a crucial role as they involved in Ras-MAP kinase pathway (Bourne, Sanders, & McCormick, 1990, 1991; Hall, 1990). The GTPases activate Ras cancerous cells require a high amount of activation of this pathway for the rapid proliferation and survival of the cells thus, enzyme modifying the Ras can be used for the treatment of cancer. Previously described studies suggest the modification of C-terminal activating enzymes of Ras to be used as drug targets for cancerous cells (Gibbs, 1991). Apart from GTPase Farnesyl protein transferase also plays a key role in cancer progression by poly isoprenylation of the group to CAXX residues on the Ras (Goodman, Judd, Farnsworth, Powers, Gelb, Glomset, & Tamanoi, 1990; Schaber, O'hara, Garsky, Mosser, Bergstrom, Moores, … Gibbs, 1990). Phosphorylation of proteins is essential. Initially, it was thought that phosphorylation was important only for the carbohydrate metabolism (Cohen & Frame, 2001). However studies of the role of phosphorylation started very early in the 80s, and researchers found that phosphorylation was an important factor for the cancer progression, one of the viral factor or Rous sarcoma virus (V-src) was found to be phosphorylation factor (Castagna, Takai, Kaibuchi, Sano, Kikkawa, & Nishizuka, 1982; Collett & Erikson, 1978). In 1980s Hiroyoshi discovered that some calmodulin binding inhibitors were found to inhibit the phosphorylation. A new generation of inhibitors found which inhibited phosphorylation by binding with CAMP and cGMP rather than binding with the calmodulin proteins. (Hidaka, Inagaki, Kawamoto, & Sasaki, 1984). Cyclooxygenases discovered in 1976. Further studies on them revealed that cyclooxygenase 2 was inducible by the proinflammatory cytokines. Both the cyclooxygenases (COX 1 & COX 2) play a role in the synthesis of prostaglandins. Nimesulide is an excellent example of COX 2 inhibitor which is used as the nonsteroidal anti-inflammatory drug (Vane, Bakhle, & Botting, 1998).

Carbohydrate metabolism is essential for any living organisms because it produces sources of energy for the survival reproduction and development of all the organisms. Parasites like Trypanosoma can evolve very rapidly making them tough to target by the immune system, so researchers decided to target the carbohydrate metabolism of the parasites to stop the infection (Opperdoes & Michels, 2001). For example, the glucose transporter of parasites govern more than 50% of metabolism of these organisms by targeting this receptor carbohydrate metabolism can be easily regulated (Bakker, Walsh, Ter Kuile, Mensonides, Michels, Opperdoes, & Westerhoff, 1999). Glucose transporter like GLUT 2 is known to play the significant role in the diabetic conditions in humans and drugs which target inhibiting the glucose transporter-like Canagliflozinare used as a treatment of Diabetes (Sarnoski-Brocavich & Hilas, 2013). NADP oxidases (NOX) are a class of enzymes essential for the phagocytic activities of macrophages, but earlier, only oxidases were believed to be responsible for the phagocytic activities. However, in the twenty-first-century, the scientist discovered the class of enzymes that playing a role in the phagocytic processes from there on the NOX became so important in the study of the immune system. There are many isoforms like Nox1, Nox2, Nox3, Nox4, Nox5, Duox1, and Duox2 which are found in humans and other isoforms are found in eukaryotes (Bedard & Krause, 2007; Krause, Lambeth, & Krönke, 2012; Lambeth, 2004). In short, the enzymes will play a crucial role in all the metabolic processes and