



REVIEW ARTICLE

ENZYME PATENTING – AN INDIAN PERSPECTIVE

Pavan Chand Akkiraju¹, Srilakshmi Mamillapalli²

1. Assistant Professor, Department of Biotechnology, P.V.P. College of Arts, Science & Commerce, Pravaranagar, Loni – 413736, Ahmednagar (Dt.), Maharashtra.
2. Department of Pharmacy, Sarada College of Pharmaceutical Sciences, Kondakavuru, Narasarao pet, Guntur, A. P., India.

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Corresponding Author*Dr. Pavan Chand Akkiraju****Abstract**

Enzymes and enzyme technology is a well-established branch of Science, which has broader applications in both research and Industries. Identifying a particular enzyme for the specific product development is of great concern in patenting. Patenting of enzymes in India from the past two decades is needed to be studied to understand the current status of enzyme patenting and product development. The process of reviewing the enzyme related patents could generate the information over enzyme patenting and its corresponding product development in India.

The current attempt includes the study of around 150 enzyme related patent's information from Indian context. Even though, the patenting process in enzymes has been started in 1933, it is found that, in between 1995 to 2015, over a period of 20 years there are only 58 patents were registered in relation to enzyme technology. This indicates that, there is a necessity to understand the concept of patenting and why enzyme technology is not able to patent more, even in the availability of advanced technologies. The current study focuses on the reasons, problems and suggestions related to patenting enzymes in Indian context.

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INTRODUCTION

The biocatalysts, commonly known as 'enzyme' (means, 'in yeast' *Greek*) were first crystallized by James B. Sumner (1937) and the corresponding enzyme was named as *urease*. In the following work, he isolated and crystallized *catalase* enzyme. The consequent enzymes, which perform the function of protein digestion from polypeptide stage to small peptide stage mainly, identified and purified, were *pepsin*, *trypsin*, *chymotrypsin*, *carboxypeptidase* and *NADPH oxidase*. These biocatalysts are capable of catalyzing various metabolic pathways in the living cells of different animals. Due to this role, enzymes are considered as crucial elements in humans lives. The enzymes speed up the rate of reaction and attain the equilibrium of body. The enzyme activity requires less energy to complete the process of catalysis. The enzymes perform highly specific reactions and their degree of catalysis mainly depends on the type of substrate on which are acting. The property of enzyme specificity saves the cellular energy during metabolisms and prevents the accumulation of metabolic products, which may turn into toxic to the cell viability.

In metabolic pathways, enzymes can act as *oxidoreductases*, *transferases*, *hydrolases*, *lyases*, *isomerases* and *ligases*. These enzymatic reactions deal with the major biochemical reactions, i.e. anabolic, catabolic and oxidation-reduction reaction at cellular level. The internal collaboration between the enzymatic activities completes the entire

metabolic pathways of a cell. The product of a particular substrate can become a new substrate for new metabolic pathway. This is how, the cells maintains their stability and balance in controlling all the metabolic pathways.

Industrial Applications of Enzymes

By remaining in cells and functional towards the life, enzymes also plays significant role in developing industrially important products. They play vital role in developing certain products that are used in day-to-day life. The industrial sectors, that are essentially dependent on enzymes include, brewing, textiles, animal feed, baking, etc. The list of these industries in vast and can be extendable. The detergent manufacturing industry utilizes the enzymes *proteases* (protein degradation), *cellulases* (cellulose degradation), *lipase* (fats degradation) and *amylase* (starch degradation). The starch processing industry involves the use of *amylase* and *glucoamylase* (starch to glucose conversion) and *isomerase* (Hugh fructose syrup). The other enzymes with great industrial importance include *proteases* (tanning, animal feed), *amylases* (baking, textiles), *hydrolases* (gas and oil), etc.

The identification of enzymes and its consequent product from a specific product involves the identification of enzyme, followed by their extraction and purification. In general, industries make arrangements to continue the mentioned process, as the role of enzymes in the development of new products is well known. Current day scenario in industries has no boundary in extending their efforts, not only to develop a novel product, but also patenting the same to get the complete benefits of the product.

Patents & Patenting

A patent is the whole right of the patentee towards the innovative ideas or product for a limited time period. A patent has to be granted by the government body of that particular country, where the patent application has been filed. The norms and conditions of patent issuing body may vary according to the global, cultural and environmental conditions. Patents are a form of tangible representations of novelty of a product. The other forms of intellectual property include geographical indications (GI), copy right, etc. Any patent, which is accepted by the governing body to be patented, is highly protected and the inventor or his representatives hold the right of the patent. Infringement of these rights may be giving origin to more problems and sometimes leads to imprisonment also. The general process of patent includes the information from the investor, followed by his patentability search. If the patent is not found on his specific invention, the patentee can file for his patent in the corresponding patent office. Following the patent application, the patent issuing office should send the application for various levels of examination to clarify about the product's novelty and other parameters of innovation. Once the process of application is terminated, the product may be accepted to get patented or amended.

The Indian patent system has evolved during a period of around 150 years to have a structured or ordered manner of patenting. The sequence of the advancements in Indian patent system is given in Table - 1 (Source: <http://ipindia.gov.in/ipr/patent/patents.htm>).

Patents in Enzymes and Enzyme technology

The enzymes and enzyme technologies are of great importance due to their industrial applications. It is possible to identify and study the problems, reasons, solutions and patent information related to them, if a constant and standard method of research is applied. This will provide useful information to the Society, which can increase the patentability of enzymes and enzyme technologies in India. The current review focused on study of enzymes which are patented under Indian Patent system and also to study, how many enzyme products are commercialized at regular intervals and continuing in the market, following their patenting. This information is achieved by studying the number of patents filed and granted for enzymes and enzyme technology in India. The study also extended to identify the patented enzymes, which may be developed into commercial products. In this connection, a total of 150 patent's information was collected to review their date of application, acceptance and other related information from the web site of ipindia.gov. These patents are solely from Indian Scientists or Industries or Organizations or individuals (Table – 2).

Analysis of Patent filing for enzymes:

Even though there are many number of patents are registered worldwide, the patents for enzymes are significantly less. The Indian companies or individuals holding patents for enzymes or enzyme technology are also found to be in very small number. From the past two decades, only fifty eight (58) patents were registered and accepted for enzyme related patents.

Analysis of Patents Accepted for enzymes

The current analysis has focused on the patents associated with enzymes and enzyme technology from the past two decades. There was only one patent issued during 1998 and 1999. The consequent years 2000 and 2001 are a little encouraging and each year issued three patents. The consequent years i.e. 2002 (4), 2003 (8), 2004 (8), 2005 (7), 2006 (2), 2007 (2), 2008 (4), 2009 (1), 2010 (11), 2011 (3) showed a rise in the process of enzyme patenting. In the year 2010, there were a maximum number of eleven (11) patents registered and accepted for enzymes and enzyme technology. But, after that, the enzyme patenting again started to minimize the number.

Analysis of Patents filing and accepting for enzymes

The patents related to enzymes and enzyme technology from the year 1998 to 2015 showed that there are only 58 patents were accepted over a period of sixteen years, with an average of only four patents per an year. The number of patents issued is summarized in figure 1. From graph, it is clear that, there is dramatic increase in patenting in enzymes and enzyme technology from 1998 to 2005. But, later again, there was a sudden downfall in the patenting process. It is very clear that, the patenting has been increased again in the year 2010 (with 11 patents), which shows that, there is an intention again developed towards patenting for enzymes and enzyme technology. But, the following year (2011) has only three patents, showing that, the coming years may have again downfalls for patenting in this area.

Analysis of Products developed from the Patents

The products developed from the patents in enzyme and enzyme technology is very less and limited in number. The number of patents in this specific area is found to be very less. So, the number of patents turning to the products is also highly limited. There are only a small number of products like enzyme containing kits and a small portion of enzyme bottles are available for laboratory purposes. There are so many enzymes, which are not patented or patentable.

The major governing bodies like Council for Scientific and Industrial Research (CSIR), Department of Biotechnology (DBT), Defense Research & Development Organization (DRDO) and Department of Science and Technology (DST) are mainly involved in enzyme patenting.

There is very limited number of Private Industries or Organizations, showing interest in enzyme patenting. Even though, there are many companies, who are working with enzymes and developing kits in Immunology and other Biochemical areas, the number of patents applied seems to be very less comparatively.

DISCUSSION

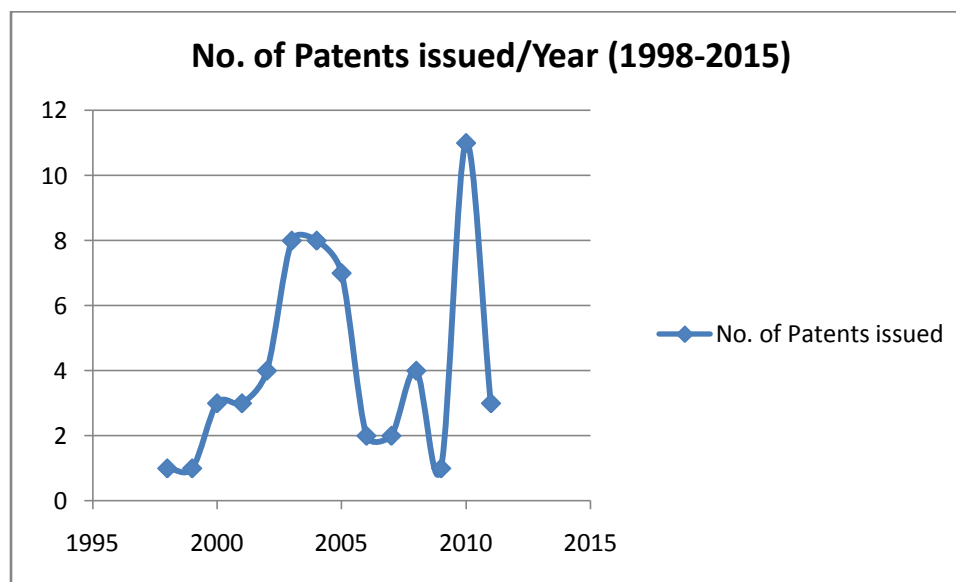
The patenting process for the enzymes and enzyme technology is found to be one of the most important areas of research. The enzymes, being the catalysts of many biological reactions are of great importance in the research point of view.

According to the data given above, only a small portion of enzyme research has been patented, showing the intension of maintaining the secrecy of the enzymes. But, the vast number of research results is not getting patented. From the data, it is clear that the patents from this particular area are very less in number. And even, from India, the number is further less. From the above mentioned data, there are only three to four patents issued per year in India.

The important aspect of product development is mainly relies on the cost effectiveness. In India, only some of the Government bodies like CSIR, DBT, DST, DRDO or any National organization that is involved in Research can get relevant amount to apply for patents for the invention. In this case, the small organizations and individuals, they may not get support in any manner to apply for patenting of their invention. This is the area, where a lot of progress has to be done.

Even, the private companies are not interested to go with the process of patenting, unless they observe any great benefit over the patenting process. If the profit is only in limited value, the companies may not show interest in patenting.

If the organizations are capable and their invention is of great importance, it is always preferable to get the patents. Even, the profit is less, but, it may be beneficial to the organization in nearby future.

Figure 1: Graphical representation of patents for enzymes and enzyme technology during 1998 to 2015**Table 1- Historical prospects of patent laws in India**

Year	Patent Law
1856	The Act VI of 1856 on protection of inventions based on the British Patent Law of 1852. Certain exclusive privileges granted to inventors of new manufacturers for a period of 14 years.
1859	The Act modified as Act XV; Patent monopolies called exclusive privileges (Making, selling and using inventions in India and Authorizing others to do so for 14 years from date of filing specification).
1872	The patterns and Designs Protection Act (Act XIII of 1872)
1883	The Protection of Inventions Act.
1888	Consolidated as the Inventions & Designs Act.
1911	The Indian Patents & Designs Act.
1972	The Patents Act (Act 39 of 1970) came into force on 20 th April 1972.
1999	On March 26, 1999 Patents (Amendment) Act, (1999) came into force from 01-01-1995.
2002	The patents (Amendment) Act 2002 came into force from 20 th March 2003.
2005	The patents (Amendment) Act 2005 effective from 1 st January 2005.

Table 2- Patents of enzymes and enzyme technology during past two decades

Year	Date of Filing	Application Number	Applicant/ Inventor Name	Title of the Invention	Publication Date
1998	17/03/1998	439/CAL/1998	Shelley Bhattacharya	A Process for the preparation of immobilized enzymes	23/10/2009
1999	19/04/1999	604/DEL/1999	DST & IIT (Munishwar Nath Gupta <i>et al.</i>)	A process of producing enzymes with enhanced catalytic activity	16/01/2009
2000	11/12/2000	1071/MAS/2000	C.S. Sainathan,	Cattle Pregnancy detection test kit employing pencillinase enzyme	28/05/2010
2000	31/03/2000	302/MUM/2000	Lupin Laboratories Ltd. (Singh Rupender <i>et al.</i>)	An antigenic peptide for use in HIV diagnosis and an enzyme immunosorbent assay comprising the	01/07/2005

				same	
2000	28/03/2000	331/DEL/2000	CSIR (Vinod shanker Dubey <i>et al.</i>)	Process for the extraction of a novel and stable esterase enzyme from a natural source	28/09/2007
2001	31/01/2001	110/DEL/2001	CSIR (Mukund Vinayak Deshpande <i>et al.</i>)	A method for preparation of Mycolytic enzymes containing mainly chitinase	12/05/2006
2001	27/02/2001	189/DEL/2001	Ranbaxy Laboratories Ltd. (Deepak Murpani <i>et al.</i>)	A process for preparing fast dissolving tablets of cyclooxygenase-2 enzyme inhibitors	29/08/2008
2001	12/03/2001	271/DEL/2001	CSIR (Varsha Bhikoba Ghadge <i>et al.</i>)	A Process for the purification of Pencillin-G acyclase from crude enzyme extract	01/08/2008
2002	17/06/2002	652/DEL/2002	CSIR (Arun Kumar, Rajesh <i>et al.</i>)	A novel cholesterol enzyme electrode	27/04/2007
2002	17/06/2002	654/DEL/2002	CSIR (Arun Kumar, Rajesh <i>et al.</i>)	A process for the preparation of novel enzyme electrode	27/04/2007
2002	31/01/2002	82/DEL/2002	National Research Development Corporation (Krishna Gopal)	A process for preparing cellulose and protease enzyme complex cud liquor form cattle and buffaloes cud for biodegradation of organic materials	21/10/2011
2002	25/10/2002	IN/PCT/2002/01498/MUM	Astraeze Neca AB. (Sunita Maria Desousa <i>et al.</i>)	Assay for detection of Transferase enzyme activity in drug screening	11/9/2004
2003	17/02/2003	00178//DEL NP/2003	CSIR (Pradeep Nahar <i>et al.</i>)	A rapid method for enzyme linked immunosorbant assay	03/08/2007
2003	17/02/2003	00178/DELN P/2003	CSIR (Pradeep Nahar <i>et al.</i>)	A rapid method for microwave mediated enzyme-linked immunosorbant assay	16/03/2007
2003	19/02/2003	154/DEL/2003	CSIR (Alankar Arun Vardya <i>et al.</i>)	Thermoprecipitating polymer containing enzyme specific ligands, process for the preparation thereof, and use thereof for the separation of enzymes	16/03/2007
2003	10/10/2003	1604/CHENP/2003	Biocon Limited (Ranganathan, <i>et al.</i>)	A process for the preparing a novel enzyme preparation for improved baking quality	23/11/2007
2003	19/02/2003	154/DEL/2003	CSIR (Alankar Arun Vardya <i>et al.</i>)	Thermoprecipitating polymer containing enzyme specific ligands, process for the preparation thereof, and use thereof for the separation of enzymes	16/03/2007
2003	12/03/2003	280/DEL/2003	CSIR (C.Rose, L.Suguha, <i>et al.</i>)	A novel process for total time and sulphide free unhairing in skins or hides using animal and/or plant enzymes	27/04/2007
2003	26/03/2003	438/DEL/2003	CSIR (Munna Singh Thakur <i>et al.</i>)	A Process for the preparation of thermostat able enzymes of high transition temperature	27/04/2007
2003	27/03/2003	478/DEL/2003	CSIR (Lalitha Ramakrishna Gowda, <i>et al.</i>)	A process for the preparation of Angiotensis converting enzyme (ACE) inhibitors	27/04/2007

2004	01/10/2004	1015/CHE/2004	Orchid Chemicals & Pharmaceuticals LTD. (Pamulapati Ganapati Reddy <i>et al.</i>)	Improved process for the preparation of coenzyme Q10	27/07/2007
2004	20/02/2004	394/DEL NP/2004	CSIR (Sreekantayya <i>et al.</i>)	A process for the preparation of Pacha Taint free tea using enzymes	10/03/2006
2004	08/03/2004	582/DEL NP/2004	CSIR (Rakha Hari Das <i>et al.</i>)	A simple efficient and accelerated process for enzyme-catalyzed invitro modification and synthesis of nucleic acid	06/03/2009
2004	12/01/2004	52/DEL/2004	National Research Development Cooperation, Malladi Drugs & Pharmaceuticals Ltd. (Perurmadom Ramaiyer Mahadevan <i>et al.</i>)	Novel thrombolytic enzyme useful for dissolving blood clots	29/12/2006
2004	22/03/2004	545/DEL/2004	CSIR (Subbaiah <i>et al.</i>)	A process for preparation of thermostable enzyme from Horsegram (<i>Dolichos biflorus</i>)	26/12/2008
2004	22/03/2004	566/DEL/2004	Tulasi Satyanarayana <i>et al.</i>	Novel amylopullulanase enzyme from novel thermolabile bacteria, <i>Geobacillus thermoleovorans</i> and process of preparing the same	26/05/2006
2004	23/06/2004	605/CHE/2004	Amodu Pharmaceuticals (H.K.Nanjaiah)	Novel synergistic lecithin with coenzymes nutritional supplement/Additive composition for poultry feed and a process for manufacturing the said composition	02/06/2006
2004	23/08/2004	838/CHE/2004	Orchid Chemicals & Pharmaceuticals LTD. (Micheal Durairaj <i>et al.</i>)	Modified expandase enzyme and its use	14/08/2009
2005	25/01/2005	0157/DEL/2005	DRDO (Karna Venkata Ramana, <i>et al.</i>)	A process for the preparation of thermo stable B-Galactosidase enzyme	6/10/2006
2005	25/01/2005	0158/DEL/2005	DRDO (Karna Venkata Ramana, <i>et al.</i>)	A process for the preparation of vegetarian medium for producing thermo tolerant B-Galactosidase enzyme	6/10/2006
2005	31/03/2005	0722/DEL/2005	CSIR (Sumant Phadtare <i>et al.</i>)	A process for the immobilization of enzymes	12/01/2007
2005	31/03/2005	0761/DEL/2005	CSIR (Lalitha Ramakrishna Gowda <i>et al.</i>)	An angiotensin converting enzyme peptide inhibitor	31/08/2007
2005	08/09/2005	2412/DEL/2005	DRDO (Karna Venkata Ramana <i>et al.</i>)	A temperature controlled immobilized enzyme bioreactor	29/01/2010
2005	20/10/2005	2810/DEL/2005	NIPER (Anirban Benerjee <i>et al.</i>)	A novel nitrilase gene from <i>Pseudomonas putida</i>	2/10/2009
2005	15/12/2005	3379/DEL/2005	CSIR (Bellur Chayapathy <i>et al.</i>)	The capsaicin synthase enzyme and an isolated gene encoding the said enzyme obtained from placental tissues of	02/10/2009

				Capsicum Spp.	
2006	20/12/2006	2726/DEL/2006	NIN & IISC (Avadesha Surolia <i>et al.</i>)	Synergistic composition for modulating activity of substrate analogs for NAD ⁺ , NADP ⁺ , NADH or NADPH dependent enzymes and process thereof	01/08/2008
2006	22/03/2006	761/DEL/2006	CSIR (Dipak Prajapati <i>et al.</i>)	A novel enzyme mediated process for the preparation of 2-aminobenzophenones	24/02/2012
2007	13/11/2007	2378/DEL/2007	CSIR (Mukund Vinayak Deshpande <i>et al.</i>)	A enzyme composition for controlling investment of woolly aphid and sooty mould on sugarcane plant and a method of treatment thereof	19/06/2009
2007	21/06/2007	903/KOL/2007	University of Calcutta (Sarkar <i>et al.</i>)	Microencapsulated enzyme biosensor for pesticide	03/04/2009
2008	08/10/2008	2161/MUM/2008	VB Medicate Pvt Ltd.)Gupta Munishwarnath <i>et al.</i>)	A stereoselective enzyme alcohol dehydrogenase converting glycerol to D-glyceraldehyde extraction, purification and characterization	30/07/2010
2008	25/01/2008	217/DEL/2008	Mahajan; Lalit	An enzyme immunoassay device for the detection antibodies and HCV antigens and a process thereof	06/02/2009
2008	19/02/2008	416/DEL/2008	Mahajan; Lalit	An enzyme immunoassay device for the simultaneous detection of antibodies and HCV antigens and a process thereof	16/01/2009
2008	21/04/2008	777/MUMNP/2008	Pharmed Medicare Pvt. Ltd. (Ratnam <i>et al.</i>)	Enzyme catalyzed deacylation of chlorinated sugar derivatives	13/06/2008
2009	25/08/2009	1750/DEL/2009	Mahajan; Lalit	A flow through enzyme immunoassay kit for the screening of HIV 1, HIV 2 antibodies for early detection of HIV 1 P24 antigen	03/12/2010
2010	13/05/2010	1115/DEL/2010	Paikray, Sitaram Prasad	Novel enzyme feed additives and animal feed with improved nutritional value	09/12/2011
2010	28/07/2010	1760/DEL/2010	Abhishek Narain Singh	Method to By-Pass allosteric domain activity of an enzyme so as to Lter the feedback or feed forward inhibition or activation	17/02/2012
2010	31/08/2010	2065/DEL/2010	CSIR (Madanala Raju <i>et al.</i>)	A novel tailor-made CU/ZU superoxide dismutase (SOD) enzyme and a process for production of the same from an isolated polynucleotide from the plant <i>Withania Somnifera</i>	02/03/2012
2010	27/10/2010	2563/DEL/2010	Akums drugs & Pharmaceuticals Limited (Sanjeev Jain)	Pharmaceutical composition containing statins, coenzyme Q-10 and Vitamin D3	04/05/2012
2010	23/11/2010	2782/DEL/2010	JIIT (Sudha Srivasastava <i>et al.</i>)	Thermally stable enzymes with improved biocatalytic activity and a process to prepare the same by making their nanoparticles	16/12/2011

2010	28/07/ 2010	1760/DEL/20 10	Abhishek Narain Singh	Method to by-pass allosteric domain activity of an enzyme so as to alter the feedback of feed forward inhibition or activation	17/02/2012
2010	31/08/ 2010	2071/DEL/20 10	ICGEB (Yazdani <i>et al.</i>)	Plant cell wall hydrolyzing enzymes from insect mid-gut bacterium	23/08/2013
2010	15/03/ 2010	589/DEL/ 2010	Prakash <i>et al.</i>	Production of extracellular enzymes from grain seeds	25/05/2012
2010	09/02/ 2010	337/MUM/20 10	Babubhai C. <i>et al.</i>	Composition and Method of preparation of fungal based bio-insecticide from combination of <i>Metarhizium anisopliae</i> , <i>Beauveria bassiana</i> and <i>Verticillium lecanii</i> fungus with enzymes, fats and growth promoting molecules for controlling various foliage pest and soil borne insect	21/05/2010
2010	25/03/ 2010	799/CHE/201 0	Microcore research laboratories India Pvt. Ltd	Methods of using enzymes and chemicals to hydrolyze baggase and egg albumin waste for the cost effective production of ethanol	30/09/2011
2010	01/04/ 2010	814/DEL/ 2010	DBT, Bannari Amman Institute (Saravanan)	Single stage preparation and finishing of cotton fabrics using enzymes	07/10/2011
2011	09/02/ 2011	1865/DEL/ 2010	JAYPPE University (Rajinder Singh Chauhan <i>et al.</i>)	Thermo halo-tolerant lipase by a new strain of <i>Staphylococcus arlettae</i>	09/11/2012
2011	01/02/ 2011	234/DEL/ 2011	Maharshi Dayanand University (Pundir Chandra shekhar <i>et al.</i>)	Polyvinyl chlroride surface co-immobilized with enzymes and uses thereof	03/08/2012
2011	14/01/ 2011	89/DEL/ 2011	University of Delhi, CSIR (R.K. Saxena <i>et al.</i>)	Optimized process for production of alkaline lipase enzyme from <i>Pseudomonas Sp.</i> And its applications thereof	30/08/2013

CONCLUSION

Any of research, which is having certain significant contribution to the Socio-economic impact, should be preferably patented. The biological catalysts, enzymes and enzyme technology are of great importance and they have to be patented for securing their specificity with the company's utilization. There is a very little focus has been given and there is a requirement in enzyme patenting. In India, there is less importance has been given for enzyme patenting. This has to be educated and more patenting has to be encouraged in enzyme and enzyme technology.

For encouraging patenting in this particular area, the Indian Government and other funding agencies should help the investigators by providing the essential funding. There by, the process of patenting would be easier and faster.

Another focus of importance is product development from the patents. This area is very weak and very less number of products is coming in to the market, after patenting. This may be mainly depending on the capability of the company to sustain in the market. The P2P area has to be strengthening by converting the patents in to useful products. This will intern decreases the cost of living in the society, by the availability of the products at regular intervals of the time.

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