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Studies on Tyrosinase Enzyme, Source, Structure production, Characteristics, Purification, and Application of Tyrosinase Enzyme

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ABSTRACT
Tyrosinase is the natural enzyme that can be obtained from the multiple sources like bacteria, fungi, plants and mammals and can only purified to a very low degree. Tyrosinase enzyme hydroxylase monophenols and oxidize O-diphnols for production of pigment(black or brown). Tyrosinase is useful in various industries such as medical, food, pharmaceutical industry and textile industry. Melanin produced due to activity of tyrosinase enzyme.

Keywords: Tyrosinase, melanin purification, characterization, medical application.

Tyrosinase(EC1.14.18.1)isacoppercontaining enzymeina75KdglycoproteinknownasmoleculeT4whichisessentialformelanogenesisandpigmentation(Claus&Decker,2006).

Tyrosinasearenearlyubiquitouslydistributedinalldomainsoflife.ithasbeenextracted,isolated,and purifiedfromvarioussourcessuchasanimals,plants,insectsandmicroorganisms(sarataleetal.,2011).streptomycestyrosinasearemostthouroughlycharacterizedenzymeofbacterialorigin(katoaetal.,2006).

Tyrosinaseisresponsibleforthe formationofmelanin(MahmoudAl-Reweidi,2017).melaninisresponsibleforthecolourofeyeshairandskininhumansitwasfirstidentifiedandnamedbytheFrenchchemistGabrielBertrandwhilestudyingtheblackeningofmushroom.melaninplaysroleintheprotectionofcellwallafteranyphysicaldamagetyrosineisinvolvedinneurodegenerativedisorderssuchasParkinson'sdiseaseandalsoincausingmelanin-Browningreactionsimportanttothecosmeticsandfoodindustries[seetraram&Saville2002]

Theenzymeismainlyinvolvedintwodistinctreactionsofmelaninsynthesis.firstly,thehydroxylationofamonophenolsecondly,theconversationofanO-diphenoltoO-quinoneundergoesseveralreactionstoeventuallyformmelanin.(Fairleadandthony-mener-2012)

Tyrosinaseareexploitedforavarietyofbiotechnologicalandenvironmentalapplicationsandthushaveattractedvariousgroupsactivelyengagedinmolecularcharacterizationandbioengineeringstudies(jusetal; 2008).

Allthesefeatureshavemademicrobialtyrosinasesasuitabletoolfortoday'spharmaceuticalfoodbioprocessingandenvironmentalTechnology.

Tyrosinase specifications:- Source, chemical structure and properties: -

Tyrosinaseactivitiesarewidelydistributedinalldomainsoflifefrommicroorganismtomammals(KamalUddinZaidi,2014).itcanbeobtainedfromvarious microbeslikebacteria,fungi,plants,andanimals.oneofthemanysourcesoftyrosinaseismushrooms.

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Sources	Species	References
Bacteria	Rhizobium, Symbiobqotrriumthermophilem, Pseudomonas Maltophiliq, Sinoehizobiummeliloti,Marinomonas, meditrrranea,thermomicrobium,Roseum, Bacillus theuringiensis, Pseudomonas putidd, Streptomyces castangeoglobiporsusRalstoniasolanaCearumVerrucomirobium Spinosum	Liu et al,2005;claus& decker 2006; McMahon et al.2007 Matobaet at ,2006
Fungi	AgaricsBoisporus,Neurooporacrassa, AspergillusOryzae,portabellaMushroom,Amanitamuscaria,lenticularBoryana,	Strothkampetal 1976 Lerch K. 1983 Nakamura et al 2000. Halaouliet a1 2005. Mueller et a11996 DeFaria et al 2007
Plants	Montrellgrape,Apple,sunflowerseed,solanummelongena,portuklaca grand flora,	Janovitz-klapp et al 1989. Tanovitz-Rlapp et al 1989. Raymond et al 1993. Lee et al, 1997 Rani et 1991,2007 '

Duetomultiplesourcesoftyrosinaseit'sstructuralpropertiesarediverseinnaturealongwiththeirdistributionintissueandcells,nocommonproteinisObservedacrossallspecies(Mayer,0006:Jaeniche&Decker,2003).structureoftyrosinasecontainbinuclearcopperIIIcenteroftwoatomscopper,everyatomissurroundedbythreeresiduesofhistidineinsidetheiractivesite(MahmoudAl-Ruweidi-Abdirahmansaid,2017).

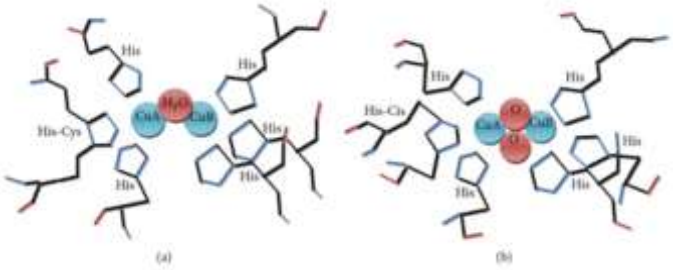

Fig- Structure of tyrosinase enzyme (Ali Nawaz et al.,2017).

Biochemical characteristics of tyrosinase enzyme

In this section we provide a brief outline of biochemical characteristics of the tyrosinase enzyme. Tyrosinase enzyme shows substrate specificity, where a higher affinity for the L-isomer of substrate than D-isomer(Kamal et al.,2014). It can be oxidise a wide range of p-substituted mono

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and diphenolic compounds(Klabunde et al., 1998). For measurement of tyrosinase activity L-Tyrosine and L-DOPA are typical monophenolic and diphenolic substrate of tyrosinase most commonly used. Tyrosinase are capable of oxidizing a variety of aromatic amines and o-aminophenols (Toussaint and Lerch 1987, Rescigno et al., 1988, Munoz-Munoz et al., 2011). It also oxidise larger compounds, which contain tyrosyl residue such as peptides, catechins and protein (Selinheimo et al., 2007Mattinen et al. 2008a, Mattinen et al., 2008b).

Table 1 Tyrosinase of different origins

Source	Molecular weight(Kda)	PH	References
Gram Positive Bacteria			
Streptomyces Glaucecens	30.9	-	Larch and Ettinger [19972]; Kim and 2005
Streptomyces Antibiotics	30.6 14.9	7.17 6.54	Katz et al[1982] Claus and decker [2016]
Streptomyces Arermitilis	33.5 13.6	9.33 6.64	CLAUS AND DEKAR [2006]
Streptomycesnigrifaciens	18	-	Nimbudiri et al [1972]; Claus and decker [2006]
Streptomyces castaneoglobisporus	31 13	6.20 6.42	Matoba rt al [2006]
Streptomyces Coelicolor	33.1 19.3	9.33 6.69	Claus and decker [2006]
Streptomyces Griseus	35.5 13.7	8.90 11.8	Claus and decker [2006]
Streptomyces Lincolnesis	30.7 14.2	6.84 7.10	Michalik et al [1975]; Claus and decker [2006]
Streptomyces larendulae	31 17	6.8 11.9	Claus and decker [2006]
Streptomyces tanashinsis	31.3 12.5	6.84 9.93	Claus and decker [2006]
Streptomyces Sp_KY -453	29	9.9	Yashimoto et al [1985] Claus and decker [2006]
Streptomycesmichiganesis	32 34.5	9.0	Philipp et al [1991] Claus and decker [2006]
Bacillus cereus	28.5	5.47	Claus and decker [2006]
Bacillus Thurigiensis	16.8	4.87	Liu et al [2004] Raan et al [2005]
Cornebacterium Efficiens	46.4	5.16	Claus and decker [2006]
Bacillus Megaterium	31	-	Shuster and fishman [2009]
Gram-Negative Bacteria			
Marinomonas Mediterranea	74.5	4.84	Claus and decker [2006]
Marinomonas Mediterranea	53.1	4.85	Claus and decker [2006]
Marinomonas Mediterranean	28.6	9.89	Claus and decker [2006]
Nitrasomonas	53.9	5.26	Claus and decker [2006]

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Europaea			
Rhizobium Et al [Rh.e]	67.4	7.28	Claus and decker [2006] Cobrera-valladores
Sinorhizobium Melioti	54.1	4.65	Claus and decker [2006]
Ralstonia Solonacearum	44	8.44	Hernandez-Romero et al [2005] Claus and decker [2006]
Stenotrophomohas Maltophilia	18.6	9.27	Claus and decker [2006]
Pseudomonas Melanogenum	-	-	Yoshida et al [1974] Claus and decker [2006]
Vibri'o Tyrosinatics	38.5	-	Pomeratnz and murthy [1974] Claus and decker [2006]

Fungi			
Pychoporus Sanguneus	45	4.5 5.0	Halaouli et al [2005] Halaouli et al [2006]
Trichoderma Reesei	43.5	9.0	Selinheimo et al [1984] Halaouli et al [20061]
Aspergillus Oryzae	6.7	-	Ichishima et al [1984] Halaoali rt al [2006]
Lentinula edodes	45-55	43-4.7	Kanda et al [1996] Halaouli et al [2006]
Neurospora Crassa	46	8.3-8.5	Lerch [1983] Halaouli et al [2006]
Agaricus Bisporus	13.4 43	4.7-5.0	Lerch [1983] Halaouli et al [2006] Solomon et al [1996]

Mammals			
Human melanocyte	66.7	-	Solomon et al [1996]

Optimum Temperature-

According to previous research has shown. the optimal temperaturevalues of25°C for thymus tyrosinase [Dogan and Dogan 2004). For Bromley's seedling, apple and banana pee optimal temperature is 30°C (yang et al., 2001;Eidhan et al.,2006). Pyrogalld as substrate (Dogan and solman 2007),mango pulp (Wang et al., 2007) showed optimum temperature 30 ° c. 20 °c. optimum temperature showed by Litche- pace-paw Sweet dog rose, basil tyrosinase with catechol as substrate (Wang et al., 2007; Dogan et al., 2005).Thus it is stated that optimum temperature duge for tyrosinase are quite species and substrate dependent [Dogan et al ., 2006).

Optimum pH-

Tyrosinase activity at 30 ° c over a, pH range of 5.0-8.0 in 50 Mm phosphate buffer used to Find out effect of pH on enzyme activity. The presence of multiple form of mushroom tyrosinase abnormal pH activity profiles might be form (Jelly et al.,1969).Therefore the optimum pH of tyrosinase is highly dependent on the enzyme source and 'the nature of the substrate used. For tomato tyrosinase optimum pH was 4.8by using3,4Dihydroxy phenyl- aceticacidas the substrate (spagna el al.,2005).The optimum pH was 6.5 for banana tyrosinase using dopamine as the substrate (Rang et al.,2007).Pyrogallas the

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substrate forartichoketyrosinase which have optimum pH is 8.0 (Dogan et al .,2005).Different pHwas optimum(6.0 and 7.0) showed, by two isoform of tyrosinase from hybrid poplar by using catechol as the substrate (Wang and constable 2003).

Mechanism OF Tyrosinase Action: -

Tyrosinasecatalyzestwotypesofreactonsinthepresenceofmolecularoxygen:theortho-hydroxylationofmonophenolstoitscorrespondingO-diphenolandconversionofanO-diphenoltoO-quinoneundergoesseveralreactionstoeventuallyformmelanin(Fairheadandthony-meyer2012).

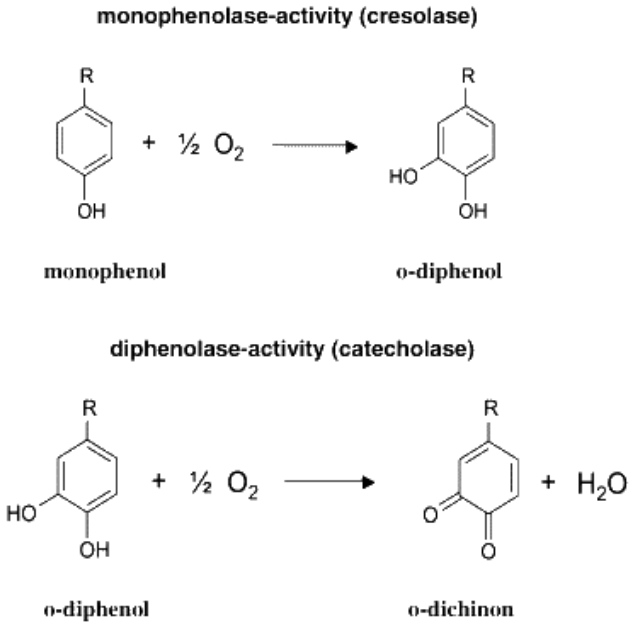

Fig:enzymaticactivitiesofTyrosinaseandrelatedcopperenzymesFrom H. Claus and H. Decker, Bacterial tyrosinases, Syst. Appl. Microbiol. 29 (2006).

Production process-

For production of tyrosinase enzyme soil sample will be collected from different sites. Among different bacterial strains a high yield. Tyrosine producing potent strains was isolated for further study.This bacterial strains were routinely grown on nutrient agar medium (Dalfard et al.,2006) at 35 ° C for 3 days then preserved at 80 ° C in glycerol. Bioprcocess is a process that uses complete living cells or their components to obtain desired product. It is a technique of biological conversions of complex substrates into simple compounds by various micro-organisms such as bacteria, fungi, and actinomycetes. (Balakaishan and Pandey.,1996). By using Response surface methodology, solid and submerged fermentation production process carried out. .

The development of suitable and standard bioprocesses has lead to industrial level production of bioactive compounds (denain1999)Solid and submerged states are conveniently referred as fermentation of bioprocesses the of extent of enzyme production is dependent on the variety of factors that are used to prepare fermentation medium compounds of medium and its environmental and physical condition (Gupta, 2002). The fermentation medium must appreciably meet the industrial requirement of fermenting organisms for better yield (Frost and Moss 1987). The media basically contains sources of carbon nitrogen and metal ions (volesky and luong 1985) Optimization strategies have been used to be provenas the key factors in developing media that fully can achieve high productivity. consistency and economical fermentation processes (Maiorella et al.,1980). Nitrogen metabolism by microorganism had recently reviewed by Payne (1980)

For the maximum production of tyrosinase well optimized media components, cultural conditions including physicochemical and nutritional parameters are most important. (Daryoush et al.,2013) optimized media Components for high and maximum product (Shivaveeraku et al.,2013) carried out for process optimization for the production of tyrosinase. In

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studies, the enhanced production of tyrosinase was carried out by processes.Optimization of physical and nutritional parameters During studies the effectof nutrition al factors were optimed which includes the effect of carbon nitrogen and metal ion source too.

Enhanced production of any bioactive molecules can normally be achieved by various physicochemical, nutritional, molecular immobilization technique and mutational regulatedoperations. The effective tools can be usedto enhance the production such as mutation, geneticengineeringand immobilization technique Recently advanced software's and bioprocess technology resulted in several highly integrated software biased technique to achieved maximum production of the end product in any of the bioprocess. Response Surface Methodology (RSM) ts the most suitablestatistical design and advanced important technique preferred to achieve the enhaneedprecautionof the enzyme (AghaeiKohazani etal., 2012). Response Surface Methodology is been extensively used to investigate the optimization at physicochemical parameters and factors of several fermentation media with various microorganism (Chang et al. 2002).By employing yeast (Mortorella et al.,2012) optimized the culture media composition for Manganeseperoxidase and tyrosinaseproduction applying a nine factor Plarekelt Bauman experimental design with statistical design.Production of L-Dopa by AspergillumsNiger was reported (Ali and Hag. 2010) and foritPlarekeltBarmandesign was employed There are few report available on the enhanced production of tyrosinase high level production of tyrosinase in recombinant (E.coli was reported by ren et al.,2013).

Asubmerged bioprocess was carried out to optimize various physicochemical & nutritional variables for the maximumproductionof tyrosinase .At laboratory scale a submerged bioprocess (Iyer& Singhal 2010) was carried out for the production of extracellular tyrosinease by Streptomyces tuirus DBZ39 in 100 ml tyrosine broth. Tyrosine broth was sterilized at 121 ° c for 15 min A 5 days old test isolate 1 ml 1 ml suspension with spare count $1x10^8$sparely was inoculated into sterilized broth & kept for incubation at 35°C for 120 hrs. in shaker incubatorat 180rpm. An enzymeassay as mentionedunder process of screening was carried out at every 24hrs.As mentioned above, for the maximum production of tyrosinase in broth under submerged bioprocess. the, important physiochemical parameters such pH, temperate and agitation speed were optimized. A principle of operating one variable at a time keeping other constants (Liu and Tzeng.,1998) wasfollowed. to record the optimum conditions The physicochemical parameters were optimized with a range of pH from 7.0 to 9.0 with increment of o.5 temperature from 30 to 50 ° C with an increment of 5^o C and agitation speed from 150-250 rpm with an increment of 25rpm.

Many nutritional variables including carbon (Starch, glucose, sucrose, cellulose and beef extract fructose se 0.2 to 1.0%) and Nitrogen (ammonium nitrate, casein, gelatine, arginine, peptone and tyrosinase from 0.2 to 1.0%) sources were optimized by one variable at- a-time approach & keeping other constant ,as mentioned earlier. Further various minerals such as $CuSo_4$, $MgsO_4$, $FeS0_4$, $MnSo_4$, KH_2PO_4 and KH_2PO_4, at the concentration from 0.01 to o.05% were also optimized. As per mentionedearlier the amount of tyrosinase produced in the medium was determined at very 24 hrs By given procedure.

Enhanced production of tyrosinase, after the manual process of optimization was carried out by following automated statistical optimization under submerged system using Response Surface Methodology(RSM) with Central Composite Design(ECD). Submerged system fermentation was carried out to understand the influence of critical process variables namely tyrosinase beet extract, gelatine&copper Sulphate. To resolve the optimum, combination of all critical variable Central Composite Design was followed (Annapurna et al., 2009). Using the Design Expert of Software, USA (ver- 7.0) the CCD of 30 runs was set Allthe experiments were carried out in duplicate and the average of tyrosinase of produced at 96 hrs.considered as the dependent variable With (ANOVA) the analysis of variance statistical and numerical analysis of model was performed. The statistical significance of the model was analysed by fisher's F-test.

The statically and numerical analysis of the model was performed by means of analysis of variance. The statistical significance of the model was analysed by fishers' F-test. it's associated probability p (F), co-relation coefficient Rand determination coefficient R^2 which explains the equality of polynomialmodelthe quadratic models were represented as contour plots (3D) &response surface curves were generated for each variable. Submerged bioprocess utilizes free flowing liquid substratessuch as molasses and broths. There is always need of Substrates to be constantly replaced / supplementedwith nutrients as the substrates are

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utilizes quite rapidly. This fermentation technique is best suited for micro-organisms such bacteria that requirehighmoisture. Thistechnique has a additional advantage that it et provide . Easier purification of the products . Generally The the Submerged fermentation is primarily usedextraction of secondary metabolites that need to be used Liquid form (Subromaniyam and Vimala 2012) factor such as specificity, initial pH, final ph, activate and inhibitor requirements, availability, cost, toxicity and ease to control the process should be taken under consideration. (Barett.,1975).

Purification of Tyrosinase enzyme

Tyrosinaseis include in omnipresent type copper enzyme which is participating invarious essential biological functions. Purification and understanding of characterization.Of the enzyme is essential for the development of its various applications. Tyrosinaseare natural enzyme purification often to onlya low degree. there are many different methodsare used for the purification microbialTyrosinase as Dehydration 'The filtered Dehydrated culture with acetone or ammonium Sulfate and calcium salt is added into enzyme and other protein Precipitation (LA Mueller et al., 1996).The roleofammoniumSulfate is also very important in enzyme Precipitation . The various concentrationofammoniumSulfatevotingfrom 35% to 70% saturated solution subsequently used . in tow steps (H Kamahldi et al.,2004) 25% - 70% (J L-Lee et al.,1997) . There are numerous methods are used for the purification of tyrosinase from different sources. Few methods are used from various species of mushrooms for the production of enzymes. (LG Fenoll et al.,1997 , S koga et al.,1992). In the process of purification of microbial tyrosinases various columns containing hydroxylapatite(s Bauchilloux et al.,1992) ,.Deae Cellulose(Y fan and WH Fluzkey 2004) or size exclusion gel (H.I.Wichers.,1996) have been performed.

Extraction of Streptomycesnigrifaciens and Streptomycesglaucescensare two species used forpurification of first bacterial tyrosinase enzyme. (AM D. Nambudiri et al.,1972 and k. Lerch Ettlinger 1997).The most eukaryotic tyrosinase the active from of the Sglaucescens protein is a monomer without tendency of concentration dependent aggregation as shown by analytical. ultracentrifugation The enzyme has a molecularmass of 29,100 Dain SDS - PAGE and its maximum activity at pH 6.8. The extra cellular tyrosinase of S glaucescens was isolated after one years form the culture supernatant (R. Crameri et al.,1982). The intro and extracellular forms were identical in their malecular masses N- terminal Sequences and cresolase/ catecelase ration. (R. Crameri et al.,1982) purified the intra and extracellular tyrosinase of Streptomyces antibiotics The multicopy plasmid pIJ702 is used amplification of the Mel gene for homologous Overexpression of the enzyme.

The molecular mass determined by SDS-PAGE and exclusion gel chromatography was 29,500 Da. The extracellular Tyrosinase of Streptomycesmichiganensis has been. isolated from a l0l fermentation broth (S Philipp, T: Held. HI kutzner, 1991).The purified enzyme exhibited two hands corresponding to 32,000 and 34,500 Da in SDS- PAGE, However, only one hand at pH 9.0 after isoelectric focussing.

The tyrosinase enzyme act with various monophenols (tyrosine, tyrosine - ester, p-Coumaric acid) and diphenols (L- dopa Caffeic acid, catchol). The enzyme from Streptomycescastaneoglobisporus has been efficiently Over expressed in EscherichiaColi. The protein purified on a Ni (II) bound affinity columns (P Y kohashi et al.,2004). FromBacillusthuringinsisis strain a heat Inducible tyrosinase enzyme purified in by one purificationstep(LN Liu, et al.,2004) With only 14 k Da This tyrosinase has lowest molecular mass the all known tyansinase enzymes A dimer is. the presumptive active from in contrast to Streptomyces tyrosinase.

Tyrosinase enzymes also found in some Gram negative bacteria from thermiocrobiumraseum a thermostable tyrosinase enzyme shows maximum activity at 70°C and pH 9.5. (k. H. Kong et al. 2000). The active forms found to be a Home dimer of two 43,000 Do subunits. From Marino monas Mediterraneanintracellular tyrosinase enzyme is formed which is found in marine water called marine bacteria and (D. Lopez et al. 2002) othertyrosinase enzyme purified from Vibrio tyrosinaticus . (Š H. Pamerantz and V.V. Murthy 1974) and demonstrated in Pseudomonas melanogenum(H.Yoshida et al.,1974).

In eukaryotic organisms, there are no reports about process of post translation, for Bacterial tyrosinase enzyme e,g, proteolytic activation of proenzyme.

The purification of the pure form of enzyme is very essentialand important process The crude enzyme purified by various. methods of extraction and purification, such as.Salt

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precipitation Dialysis. Gel filtration Ion exchange chromatography etc.

All process carried out serially- So as toproduce the enzyme in its purest form.The obtained pure enzyme is used for the further analysis.

- Salt precipitation:[Http//en.wikibooks.arg]

Under ice cold condition, the crude extract was used for the precipitation with ammonium Sulfate till the saturation point.

The procedure is not only help the pure protein to get precipitate but also enables the extracted protein to retain its function.

- Dialysis:[Small, Hamish 1989 and http/www.sciencedirect.com]

The Enzyme purification most commonly accomplishedthrough the additionof a small epitope tag to the target protein fallowed by. isolation via solid - state purificationusingan is appropriate column.

The precipitate obtained in its previous stepdialyzed against normal. water so as to filter out the particularimpurities by dialysis.

- Ion exchange chromatography[Skoog D.A Thompson Brooks Cole Belmont 2006]

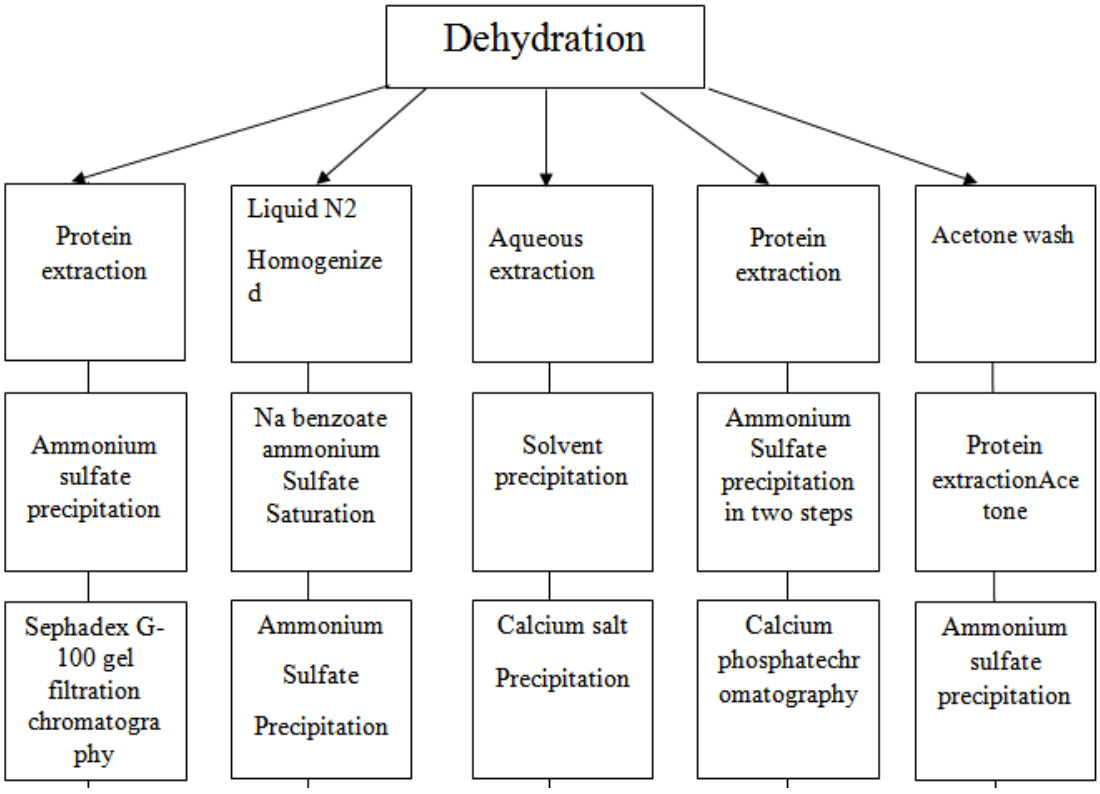
This step would enable the removal of the charged impurities The purification is achieved in one step based on principle of charge based. flatiron DEAF cellulose membrane has been used for the purification.

- Gel filtration Chromatography[http://Conductscience.com]

This step recovered the final and complete purification of the protein

The method can be used to separatecompounds Such assmall molecules, proteins, protein, complexes, polysaccharides and nuclear acids when in aqueous solution it is also used for fractionation of molecules

Sephadex G-75 is a gel filtration media used in gel filtration chromatography and protein chromatography {[https i www.sigmaaldrich com] enzyme purification is of great importance in to acquire knowledge about structural and functional properties and its applications.



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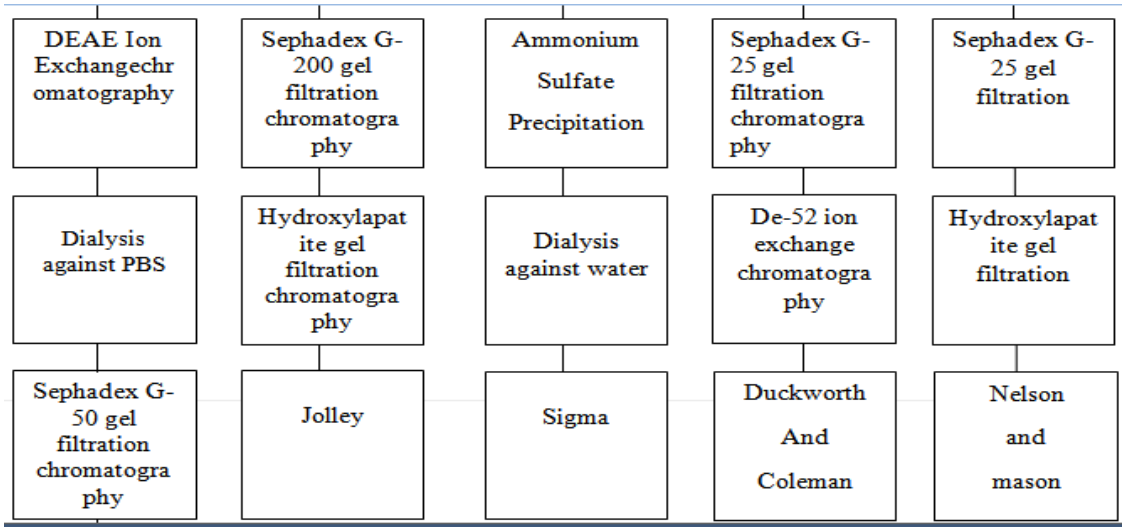

Fig-Methods for the purification of tyrosinase. Adopted from (Zaidi et al., 2014).

Application of tyrosinase enzyme :-

Medicinal application :-

Tyrosinase enzymes are omnipresent in nature and are considered one of the fundamental enzymes which are involved in several biological function and defense mechanism (Especially in melanogenesis) tyrosine related melanogenesis is responsible for pigmentation in hair, skin, eyes in mammals as pigmentation is a pivotal part of skin protection from UvRadiation(Ando et al .,2007).

In microbial world its use is still unknown melanin helps in for motion of reproduction origins& spores and cell wall protection after physical damage. The enzyme also plays important rule in melanin synthesis for therapeutic, purposes, L-Dopa production, drug utilized to treat Parkinson's disease manufacturing, lincomycin &treating various neurological disease(valipour is burhan 2016) mushroom tyrosinases is used to treat vitiligo(seoet al .,2003).

Fields	Applications	References
Food industry	In cereal processing to improve baking in order to make better volume & crumb stir of bread.	Facio,2011
Food industry	In dairy processing to cross link various dairy proteins	Selinheimo 2008
Food industry	In meat processing for improvement of gelation.	Selinheimo 2008
Medical field	As prodrun in immunoassays & antibody microarrays, to produce L-DOPA & to treat neurological problems.	Selinheimo 2008 Valipoure Burhan 2016, Zaid et al 2014
Textile industry	To modify the wool fibres & produce of diff dyes.	Selinheimo 2008, Valipoure Burhan 2016,
Cosmetic industry	As aself tanning agent	Selinheimo 2008 Valipoure Burhan 2016,
Environmental significance	As biosensors to detect the toxic phenolic compounds	Selinheimo 2008, singh N & Singh J 2002

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- It has been proposed that melanin has a role in the formation of reproductive organs & spores and in cell wall production after physical damage (Lerch,1983).
- In soil Environmental extracellular after are probably involved in polymerize & detoxication of humic matter (Claus & fillip 1988, Kutzenr 1968, Claus & fillip 1990).

Melanins bind have metals that are otherwise toxic to cells (butler & Day 1998) they also confer protect against oxidants heat enzymatic hyodrolysis antimicrobial compounds & phagocytosis & thus can contribute to microbial pathogenesis (Nosanchuk&casaclevell 2003).

Tyrosinase are suggested to be potential tools in treating melanoma (morrisom et al 1985,jarden et al 1999,2001). it is used applicants in environmental technology for detoxify of phenol-containing waste (Claus & fillip 1988) contaminated soils (Claus & fillip 1990) as biosensors for monitoring of phenols.

Also used in cosmetics & food industry's as biosensor because of either undesirable or beneficial oxidative browning reactions (mayer and harel 1978)

Synthetic melanin have application as protections against radiations (U.V X-Ray Gamma rays) action exchangers carrier for drugs antioxidants antiviral agents&immune organs.

CONCLUSION

Tyrosinase enzyme constitute one of the most important groups of commercial enzyme.These enzyme have ample utilization in industrial process, such as Pharmaceutical and Cosmetic and Food industries.However,thod review shows that microbial tyrosinase is a promising enzyme for Pharmaceutical and Food bioprocessing technology appraising ahe State of Knowledge about its structure ,biochemical properties,purification and production.

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