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Article

Plant cells mediated biocatalytic reduction of aryl and heteroaryl carbonyl compounds: a comprehensive review

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Biocatalysis is always considered as an efficient alternative for preparing a wide range of compounds with pharmaceutical/industrial importance. The immense popularity of biocatalysts is due to its striking features of being an environmentally benign, renewable and sustainable.In this present review, different methods of preparation of alcohols from their respective carbonyl compounds using different plant cells as biocatalysts are discussed. In addition, the importance of these alcohols in pharmaceutical industries and their methods of preparation in optically as well as chemically pure form are also discussed.

Keywords: Biocatalysis. Plant cells. Asymmetric reduction. Carbonyl compounds. Green chemistry.

INTRODUCTION

Green synthetic approach and development is one of the alternative solutions to reduce the environmental risks. In future, it will be mandatory to replace fuel-based materials with sources of biological origin while minimizing the environment degradation and their adverse effects on living organisms. In early 1990s, the US Environmental Protection Agency (EPA) coined the term 'Green Chemistry' to denote safe chemicals, developed from a small idea and transformed it into a global view to address environmental protection (Suman *et al*., 2018). The Green Chemistry is a broader concept that enhances the proper design of the chemical product and modify the synthetic process in to a whole in order to eliminate or to reduce the generation as well as the use of the hazardous substance to the human, animals and the environment where we live (Joshi, Adhikari, 2019). Green and sustainable chemistry simply means "The design, synthesis and applications of chemical techniques and methodologies used to minimize and reduce generation of feedstock, by-products, solvents, reagents that are harmful to human beings and environment" (Niwadange, 2016). In order for a chemical synthesis to be called "green," each reaction should have three green components: solvent, reagent / catalyst and energy consumption (Ivankovic et al., 2017). Some of the commonly used green solvents in the green synthesis process are water, ethyl acetate, ethanol, glycerol and its derivatives, Supercritical CO_2, dimethyl carbonate, ethyl lactate, etc. On the other hand, most of the chemicals which don't have green solvents can cause serious harm if not handled carefully. Direct contact (inhalation, skin, and eye contact) and prolonged exposure (occupational) are the two major routes of chemical toxicity to humans (Dwivedi et al., 2022; Katharina, Kunz, 2018). Another important criterion in developing a green synthetic process is the choice of a suitable method. Biological methods, in contrast to conventional chemical and physical methods, could be an alternative synthetic route due to its environmentally friendly reactions (Kharissova *et al.*, 2019). The advantages of green synthesis include intermediates/ products that are relatively nontoxic, with cost effective processing, biodegradable, ensuring a clean synthesis, readily available, renewable and more importantly with

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ability to operate under environmental benign reaction conditions.

Role of Biocatalysts in green chemical processes

In order to adopt green chemical strategies in synthetic industries, researchers promote the use of biocatalysts instead of different chemical or conventional catalysts. The use of enzymes as catalysts is just an academic speculation of the past, and in recent times, biocatalysis has been recognized and used as a very valuable tool for sustainable and cost-effective pharmaceutical production. In recent times, due to its sustainable nature, biocatalysts have opened up a new avenue for the development of green chemical processes. It has been widely reported that several multi-enzyme cascade reactions are being developed using biocatalysts, which are known to reduce the cost of the process by minimising the time and material consumption that is usually involved in conventional procedures (France, Lewis, Martinez, 2023). Several advantages are associated with biocatalysis, such as the use of biodegradable enzymatic catalysts, the limited number of synthetic steps, the mild reaction conditions, and the high enantio-, chemo- and regio- selectivities (Rossino *et al.,* 2022)**.** This review briefly describes the biocatalytic reduction of carbonyl compounds to alcohols, which are important chiral precursors in various pharmaceutical preparations.

IMPORTANCE OF OPTICALLY PURE SECONDARY ALCOHOLS IN PHARMACEUTICAL INDUSTRIES

Secondary alcohols are carbon atoms of -OH group attached directly to two alkyl/aryl groups, which may be the same or different. Chiral secondary alcohols are valuable synthetic molecules that are useful in their own way and also act as precursors to other functional groups like ethers, esters, etc. It is an important intermediate for many enantiopure pharmaceuticals and biologically active molecules. For instance, these secondary alcohols act as precursors in different drugs like atorvastatin, atazanavir, montelukast, paclitaxel side chain etc. (Patel, 2013). It has been reported that several enantiomerically pure chiral secondary alcohols are regularly used as the lead compounds in fields of organic chemistry, agrochemicals, and pharma industries. The chiral secondary alcohols can be synthesized using different strategies like kinetic resolution of racemic alcohols using lipases, reduction of prochiral ketones asymmetrically, regioselective reduction followed by ring opening reactions of epoxides etc. Among these methods, the kinetic resolution of racemic alcohols is most widely used followed by the asymmetric reduction of prochiral ketones (Chen, de Souza, 2019). In general, the synthesis of these industrially important chiral alcohols is carried out using conventional methods which involve the use of metals or expensive organo-catalysts and harsh reaction conditions (Truppo, 2017)**.** Considering the principles of green chemistry, the use of biocatalysts has emerged as a promising "green' alternative to the conventional chemical syntheses (Potdar *et al.*, 2015).

One of the most promising methods for the synthesis of organic compounds is biocatalysis. These biocatalysts play an important role in the production of various compounds in pharmaceutical industry, biotechnology and various industrial purposes. The use of biocatalyst is not only limited for these purposes but also plays an important role in cosmetic industries and waste water management. In recent times, the use of biocatalysis in pharmaceutical industries is gradually gaining momentum because of its effectiveness, cheap and eco-friendly characteristics (Abdelraheem *et al.*, 2019). Biocatalysis is one of the major key technologies utilized for the synthesis of pharmaceutically important compounds as it provides a more efficient and sustainable route (maps with United Nations SDGs 3, 6, 7, 9 & 12) to the active raw materials and products. In early years, hydrolases were widely used in the development of drugs but nowadays many catalytic enzymes are preferred for its robust, scalable and cost-effective method development (Lewis, France, Martinez*,* 2023).

Biocatalysis is the greenest technology used for the synthesis of chiral molecules due to its considerably less toxic, easily biodegradable properties. In addition, it operates under mild reactive conditions, exhibiting a high degree of regio, chemo- and stereo selectivity in various chemical reactions (Tao, Xu, 2009). The aim of using biocatalyst in organic synthesis is the formation of one stereoisomer of chiral target compound with high optical purity and yield. In recent years, the use of biocatalysis has been widely adopted for scale-up processes in chemical, fine chemicals, pharmaceutical and cosmetic industries (Eugene, Uchechukwu, Mariagoretti, 2016). Among the different biocatalysts, the use of vegetables as catalysts are gaining importance for the fact that they do not require stringent aseptic conditions or cause opportunistic infections like microbial biocatalysts. It has been observed that vegetable biocatalysts are widely used in synthesis and reduction of carbonyl compounds and to produce reduced product in great enantiomeric excess (ee) and conversion (Cordell *et al.*, 2007).

Ketoreductases (KRED) and alcohol dehydrogenases are the enzymes most commonly used to produce chiral secondary alcohols of medical significance. These KREDs are mostly present in fruits and vegetables; hence these plant materials are widely used for the bioreduction of carbonyl compounds (Adams *et al.*, 2019). These enzymes utilize NADPH as a reductant to avoid stoichiometric cofactors. These biocatalysts aim to reduce the impact on environment both in use of raw material and waste disposal as well as improve the safety profile of reactions on large scale production (France, Lewis, Martinez, 2023). In organic synthesis, the naturally available fruit juices help in the synthesis of compounds or intermediates. For instance, coconut juice is widely used in the reduction of carbonyl compounds for production of chiral alcohols. These fruits act as an excellent biocatalyst because they are less expensive, easily available and extraction of juices is obtained by simple and easy processes (Pal, 2013). Due to the increasing demand for the preparation of enantiomerically pure chiral pharmaceutical compounds in high purity, it has become a real challenge for the pharmaceutical industries to develop a safe, more sustainable, healthy and economically attractive methodologies for the production of chiral alcohols (Solano *et al.*, 2012). The present review aims to compile the literature available till date on the production of industrially important alcohols using various fruits/vegetables as biocatalysts in a comprehensive manner.

BIOREDUCTION OF CARBONYL COMPOUNDS

Reduction of aromatic carbonyl compounds to alcohols

The carbonyl compounds like 4'-bromoacetophenone and 4'-iodoacetophenone were reduced to corresponding chiral alcohols by garlic *(Allium sativum)* as biocatalyst (Figure 1). The product sample was identified by TLC and determined by ^{13}C NMR, ^{1}H NMR and IR spectral studies. The configuration of the product alcohol was analysed using a polarimeter. The presence of alcohol was confirmed by an acetyl chloride test. It was observed that the 4'-bromoacetophenone (**1**) and 4'-iodoacetophenone (**2**) was reduced to *R*-4'-Bromophenylethanol (**1a**) and *R*-4'-iodophenylethanol (**2a**) with a moderate yield (65% & 70%) as well as conversion (95% & 93%) and a good ee (90% & 86%) respectively (Bilal *et al.*, 2019a).

Another study identified carrot (*Daucus carota*) to facilitate the bioreduction of the ketone monoterpenoids present in the essential oil of *Mentha piperita* L. leading to a menthol in the sample with high selectivity. Initially the bioconversion of acetophenone to 1-phenylethanol was carried out successfully with a yield of approximately 93-98 %, but in the presence of menthol, the yield was reduced to 82 % (Souza *et al.*, 2018).

The Algerian mandarin (*Citrus reticulata*), strawberry tree (*Arbutus andrachne*) and ginger root (*Zingiber officinale)* were studied as biocatalysts for the conversion of ketones to their chiral alcohols. The bioreduction of acetophenone, 4-chloroacetophenone, thiochromanone, tetralones and chromanone showed

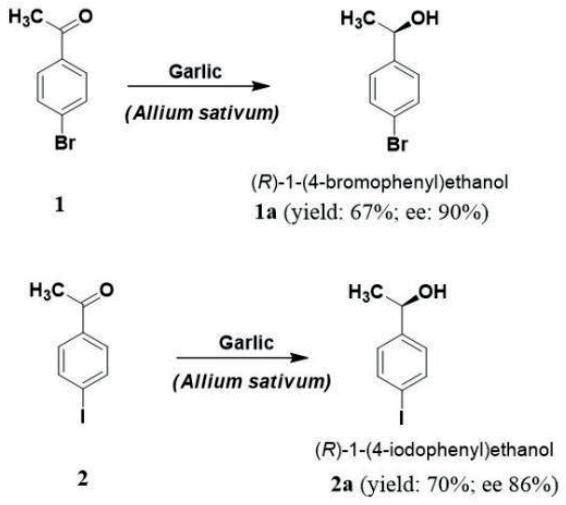


FIGURE 1 – Asymmetric reduction of substituted acetophenones using garlic.

higher enantioselectivities. The two differing batches of *Citrus reticulata* from Annaba and Skikda also acted as good biocatalysts with high enantioselectivity of 93%. The ginger and strawberry reduced the ketone to alcohols with (*S*) and (*R*) configuration and ee of 79% and 29%, respectively. The reduced products were analysed by GC and HPLC (Bennamane *et al.*, 2018).

The bioreduction of acetophenone using carrot *(Daucus carota)* was studied. The reactive products were purified and analysed using TLC and chiral GC-FID. In this study, the authors had investigated whether the surfactant Tween 20 has a role to enhance the catalytic reduction of acetophenone. Bioreduction of 4-bromoacetophenone (**1**) was carried out using carrot in the presence of surfactant 0.1% (Tween 20), led to the formation of (*S*)- 4'-Bromophenylethanol (**1b**) with a low conversion (28 %) and a good ee (96 %) and by using 1.5% of Tween 20, the formation of *S*-alcohol was increased to 67% conversion and 96% ee (Figure 2). Hence, it was reported that the use of surfactant along with *D. carota* species enhanced the biocatalytic reduction of acetophenone and its derivatives. Notably, the use of surfactants also solves the problems involved in the solubility of substrates in the reduction process (Costa, Omori, 2017).

The biocatalytic reduction of benzaldehyde to benzyl alcohol was carried out using various plant wastes as an enzyme source and the by-products were examined by Gas chromatography. The biological materials used were bean pods (*Phaseolus vulgaris*), turnip rape (*Brassica campestris* L.), lima bean (*Phaseolus lunatus*), broad bean (*Vicia faba*), and jinicuil pods (*Inga edulis*), mango (*Mangifera indica* L. cv. manila), avocado (*Persea americana*), mamey (*Pouteria sapota*), papaya (*Carica papaya*), and green apple (*Malus domestica*) peel, mamey, capulin (*Prunus serotina*), green pepper (*Capsicum annuum*), chili (*Capsicum annuum* L. var. *annuum* L. cv. 'Jalapeño') and avocado seeds (*Persea americana*)and chive leaves (*Allium schoenoprasum*). Among the biological materials tested, the most promising biocatalysts were found to be capulin (*Prunus serotina*), mamey seeds (*Pouteria sapota*) and bean pods (*Phaseolus vulgaris*), turnip rape stalks (*Brassica campestris* L.) and chive leaves (*Allium schoenoprasum*) showed good conversions (65%, 67 %, 54%, 49% and 45%) respectively (Oba *et al.*, 2017).

The bioreduction of 4'-nitroacetophenone and 4'-haloacetophenones (X=F, Cl, and Br) was investigated utilizing *Terfezia sp.* (Dessert truffles)*, Cynara scolumus L.* (Artichoke)*,* and *Phoenix dactylifer L.* (Date palm). The product thus obtained from the reduction of 4'-haloacetophenones and 4'-nitroacetophenone using *Cynara scolumus L.,* was found to have a moderate yield (29-36%) and ee (71.4-96.5%). Unexpectedly, no satisfactory result was observed with *Terfezia sp.* On the other hand, *Phoenix dactylifera L* was found to be the favourable plant tissue for the chiral alcohol production through asymmetric reduction of substituted acetophenones which was evident from its excellent yield (51.5 - 77.2%) and an ee (66 – 89%) compared to other plant tissues (Nedjimi, Sekhri, 2016).

Vegetable biocatalysts used in reducing process of ketones to their respective chiral alcohols were fresh carrots (*Daucus carota*), cabbages (*Brassica oleracea*), turnips (*Brassica rapa*), radishes (*Raphanus sativus*) and parsnips (*Pastinaca sativa*). The substrates used for

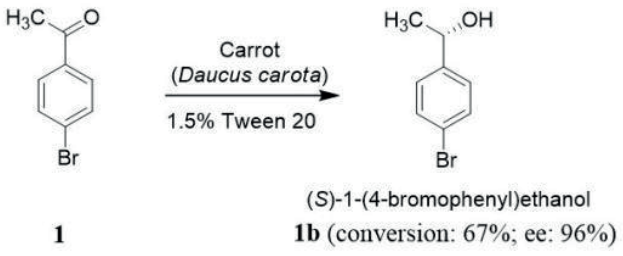


FIGURE 2 - Asymmetric reduction of 4′-bromoacetophenone using carrot.

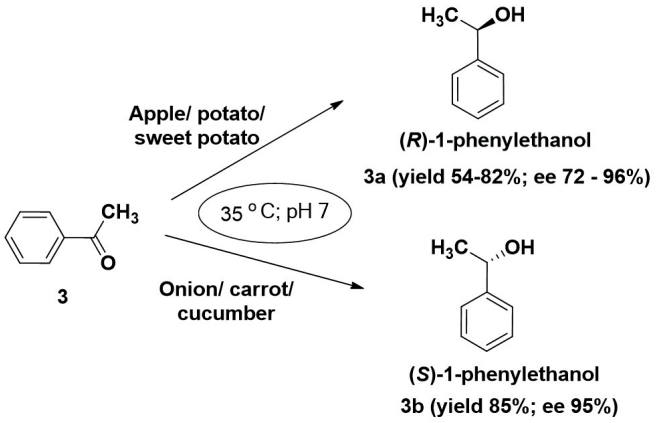


FIGURE 3 - Asymmetric reduction of acetophenone using different fruits/vegetables as biocatalysts.

the reduction include benzoyl acetonitrile, 3-chloro propiophenone, and 1-acetyl naphthalene, 2-methyl benzophenone and 4-chloro benzophenone. The chiral alcohols were obtained with good yield between 40% - 90% and excellent enantioselectivities (>99%). The products thus obtained were analysed by ^{1}H NMR and chiral GC studies (Javidnia *et al.*, 2016).

The asymmetric reduction of acetophenone to 1-phenyl ethanol was investigated using vegetables as biocatalyst and the reaction parameters were optimised using carrot as the biocatalyst. The various other biocatalysts tested in this study were apple (*Malus pumila*), cucumber (*Cucumis sativus*), onion (*Allium cepa*), potato (*Solanum tuberosum*), radish (*Raphanus sativus*), and sweet potato (*Ipomoea batatas).* All the biocatalysts reduced the acetophenone to 1-phenyl ethanol with both *R* and *S* form configurations. The best ee and chemical yield were obtained during the biocatalytic reduction using carrot and potato. The optimized reaction conditions for the asymmetric reduction of acetophenone (**3**), were 35°C and pH 7. The (*R*)-1-phenyl ethanol (**3a**) was the predominant product formed from the reduction using apple, potato and sweet potato and while other vegetables produced (*S*)-1-phenyl ethanol (**3b**) with excellent yields 54-82% and enantioselectivities 72-96%. The carrot reduced the ketone to (*S*)-1-phenyl ethanol with 85% chemical yield and 95% ee (Figure 3) (Xu *et al.*, 2010).

The enantiomerically pure (*S*)-1-phenyl ethanol and its derivatives produced from the bioreduction of acetophenone has an immense value in the pharmaceutical industry as it is used as an important chiral precursor for the anti-Alzheimer drug (Kazici, Mehmetoglu, 2015).

Using vegetables from the family *Apiaceae*, stereoselective bioreduction and enantio-separation of racemic bicyclo (3.3.1) nonane-2, 6-dione (**4**) were carried out (Figure 4). Chloroform was used to extract the (+)-enantiomer from the aqueous reaction mixture of aqueous solution while an enzymatic reduction of (−)-enantiomer produced the reaction product, i.e. 6-hydroxy bicyclo (3.3.1) nonane-2-one (**4a**). The reactive product was analysed by UPLC of PDA detector and Quadrapole and TOF Mass spectrometry. Among *Apiaceae* species the celery roots *(Apium graveolens)* showed promising results and hence the reaction time, temperature and amount of substrate added were optimized. It showed that the (+) enantiomer produced a maximum optical purity of 90-98% and an excellent yield of more than 98% (Zilinskas, Sereikaite, 2013).

Lens culinaris (lentils) seeds were used as a biological catalyst in reducing the process of aliphatic and aromatic aldehydes and ketones with moderate to good chemical yield. The ketones like acetophenone, and α-tetralone were successfully reduced to their corresponding chiral alcohols. Acetophenone showed

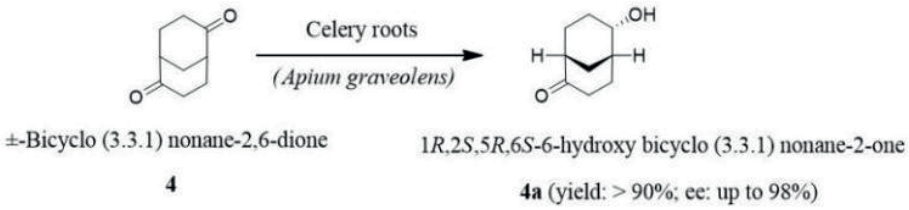


FIGURE 4 - Asymmetric reduction of bicyclo(3.3.1) nonane-2,6-dione using celery roots.

a low yield (17%) compared to other ketones which showed an excellent yield with other biocatalysts. The various aliphatic and aromatic aldehydes [cinnamic aldehyde, benzaldehyde (>99%), furfuraldehyde (>99%), *meta*-methoxy benzaldehyde (95%) and *para*-methoxy benzaldehyde (96%)] were reduced to their corresponding alcohols and the amount of conversion is mentioned in parentheses. The aldehydes were more reactive than ketones and among the ketones, aliphatic ketones showed higher activity than aromatic ketones (Ferreira *et al.*, 2012).

The Brazilian beans *(Vigna unguiculata)* whole cells act as biological catalyst in the process of reducing the acetophenone and its derivatives to their chiral alcohols with good to excellent (>99%) stereoselectivity and the products thus obtained were found to be of *R* and *S*-configurations. Enantiopure (*R*)-β-chloroalcohols was achieved with good conversions and aliphatic ketones were also reduced. The products were characterised using different spectral studies and conversion and the ee were analysed by MS, GC and HPLC techniques (Bizerra *et al.*, 2010).

The halogenated fluorenones were asymmetrically reduced to their respective alcohols using various fruits and vegetables as biocatalysts. Among many vegetables and fruits, grapes showed excellent enantioselectivity (ee: 99%) and conversion (97%). The use of surfactant (Triton X-100) not only minimise the use of dimethyl sulphoxide as the solvent but also improved the biotransformation of ketones with excellent conversion of approximately 90% but did not alter the enantioselectivity. The halogenated substituents showed higher enantioselectivity, which could be due to the electron withdrawing nature of halogens. The reduced product 2-chloro fluorenol showed *R*-configuration (ee: up to >99%) indicated that the reduction followed anti-Prelog rule (Xie *et al.*, 2009)

Earlier, the biocatalyst of coconut water *(Cocos nucifera L.)* was used in reduction of both aromatic and aliphatic ketones to their corresponding chiral alcohols with greater yield and excellent enantioselectivity. The biocatalyst also reduced the aromatic aldehydes to their respective alcohols. The juice of *Cocos nucifera* significantly reduced the aldehydes to alcohols with a conversion of 88%, ketones to chiral alcohols (*S*-configuration) with enantiomeric excess of 95-99% and esters with ee value of 99%. The purified products were further analysed by NMR and GC-MS studies (Fonseca *et al.*, 2009).

A series of aromatic aldehydes and ketones were reduced to their respective alcohols using the fruit peel of the species *Passiflora edulis* (Passion fruit). The reduced products were analysed by GC-MS, NMR and HPLC techniques. All carbonyl compounds tested were biocatalytically reduced to their corresponding alcohols with moderate to excellent conversions (30-97%). The two cinnamic aldehydes produced alcohols with conversions of 41-35% and the aromatic ketones produced the respective alcohols in varying conversions of 30-74%. The enantiomeric excess (23-64%) of two compounds were determined by chiral HPLC studies. The substrate repertoire of the reductase enzyme system of *Passiflora edulis* could be extended to aliphatic carbonyl compounds like cyclohexanone and ß-keto-ethyl-butyrate. The cyclohexanone reduction produced the corresponding alcohol with a

greater yield of 97% and the complete chemoselectivity was obtained by the reduction of ß-ketoester to their corresponding ß-hydroxyester with 81% yield. The results demonstrated that *Passiflora edulis* fruit peel has an enzyme system which is capable of reducing the carbonyl compounds to their corresponding alcohols with high conversions and good isolated yields. Low to moderate enantiomeric excess was found for the chiral alcohols and the major enantiomers showed the (*S*)-configuration (Machado *et al.*, 2008).

The prochiral ketones like acetophenone, 4-chloroacetophenone, ethyl 4-chloroacetoacetate were asymmetrically reduced to their respective alcohols (Prelog products) using various biocatalysts. The biocatalysts tested were Apple (*Malus pumila*), carrot (*Daucus carota*), cucumber (*Cucumis sativus*), onion (*Allium cepa),* potato *(Solanum tuberosum),* radish *(Raphanus sativus)* and sweet potato *(Ipomoea batatas*). The biocatalytic reduction produced alcohols with high enantioselectivity. The products were analysed by GC using a FID detector at 250°C. Using the optimized reaction conditions, the asymmetric reduction of acetophenone and 4-chloro acetophenone was carried out using the plant cells and the ee and yield of the products (*S* – alcohols) thus obtained was enhanced up to 98% and 80% respectively. Notably, the ee. and yield for (*R*)-ethyl 4-chloro-3-hydroxybutanoate was about 91 and 45% respectively using carrot (*Daucus carota*) (Yang *et al.*, 2008).

The biocatalyst like sugarcane (*Saccharum officinarum*) juice was used in the reduction of a group of compounds including aromatic and aliphatic aldehydes and ketones. The bioconversion of various aldehydes and ketones to their corresponding alcohols were identified by TLC and quantified by GC-MS using capillary column with FID detector. Acetophenone and 3-methoxy acetophenone were reduced to (*R*)-1-phenyl ethanol (ee: 56.7%) and (*S*) -1-(3-methoxy phenyl) ethanol (ee: 41%) with moderate conversion (16-39%). Good yield (up to 90%) was produced by all aldehydes except vanillin, cinnamaldehyde and α-methyl cinnamaldehyde. Among these, the aliphatic aldehydes showed 100% yield than the aromatic aldehydes. The aliphatic ketones, which was tested using this biocatalyst also produced 100% yield than the heterocyclic ketones (Assunção *et al.*, 2008).

The aromatic aldehydes (benzaldehyde and cinnamaldehyde) and aliphatic ketone (hexan-3-one) were reduced to their corresponding alcohols (benzyl alcohol, cinnamyl alcohol and hexan-3-ol,) using a *Manihot* species (*Manihot esculenta* and *Manihot dulcis*) roots. The products reduced were analysed using GC-MS and IR spectral studies. Notably, the reduced products produced an excellent yield (80-96%) and were in good ee (94-98%) (Machado *et al.*, 2006).

Enantiomerically pure 1-phenyl ethanol, finds immense applications in pharmaceutical industries. Hence, several plant cells were used as biocatalysts for the preparation of this optically pure alcohol with high yields and optical purities (Table I).

The bioreduction of aromatic carbonyl compounds to alcohols of substrate acetophenone and its derivatives with different vegetables and fruits are discussed in Table II.

Bioreduction of homocyclic and heterocyclic carbonyl compounds to alcohols

The mature fruit of *Lycopersicum esculentum L* (tomato) successfully catalysed the enantioselective reduction of imidazol-2-ones (**5**) (Figure 5) and pyrimidin-2-ones to the heterocyclic alcohols (**5a**) that are associated with them. It was shown *that Lycopersicum esculentum's* enzyme dehydrogenase selectively reduced aromatic heterocyclic ketones to their corresponding alcohols in high yields and enantioselectivity. The products were analysed by HPLC using a chiral column fitted with a UV detector at 210 nm. The reduced *S* –product showed a yield of 85-91% and an ee of 95-99% (Phukan, 2015)

In Algeria, medlar fruits (*Mespilus germanica L*) was used for the biocatalytic reduction of prochiral fused heterocyclic ketones containing thiophene, furan, chroman and thiochroman to the

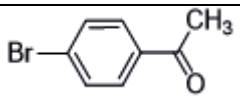
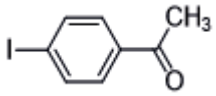
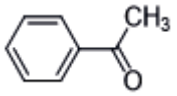
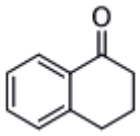
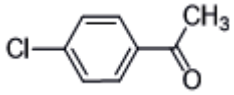
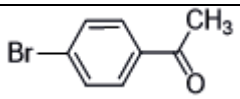
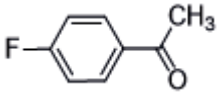
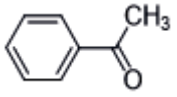
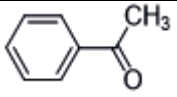
TABLE I - Asymmetric reduction of Acetophenone to 1-phenyl ethanol using different vegetables/fruits as biocatalyst

Biocatalysts used	Configuration and ee	Yield/ conversion	Reference
Phoenix dactylifera L	*R* ; 60.0-89.0%	52.0-77.2%	(Nedjimi, Sekhri, 2016)
Cynara scolumus L.	*R & S* 53.3%	30 %	(Nedjimi, Sekhri, 2016)
Daucus carota	-	98%	(Souza *et al.*, 2018)
Cucurbita pepo	*R*; 50-96%	77-88%	(Bilal *et al.*, 2019b)
Ficus carica	*R* 76% (Fresh fig)	78%	(Bilal *et al.*, 2019c)
	R 80% (Dried fig)	85%	
Phaseolus vulgaris L	*R*; 82%	38%	(Salvi, Chattopadhyay, 2017)
Manihot esculenta and Manihot dulcis	*S*; 94-98%	80-96%	(Machado *et al.*, 2006)
Ligustrum lucidum	*S*; >99%	94%	(Aimar *et al.*, 2014)
Phaseolus vulgaris (Ispir beans)	*S*; 99%	40%	(Atak, Bayraktar, Mehmetoglu 2019)
Sinapis alba	*R*; 53% (with PVP)	68.5% (with PVP)	(Sousa *et al.*, 2019)

relevant alcohols was discussed. The medlar fruit reduced the ketones with an excellent ee of 98%. A higher enantioselectivity was noticed in tetralone and thiochromonone with an ee of 89% and 98%, respectively. A good biocatalytic method was developed for chromanone using different parts of medlar fruit showed an ee of 77%. (Bennamane, Zeror, Zouioueche-Aribi, 2014). Thus, *Mespilus germanica* fruit could be considered as a promising biocatalyst for the reduction of various ketones.

The asymmetric reduction of substituted heteroaryl methyl ketones to their respective chiral alcohols using carrot (*D. carota*) was investigated. Substituted heteroaryl ketones had pyridines, pyrrole, furan and thiophene as the heterocyclic moiety. The reduced products were identified and yields were determined by

TABLE II - Summary table of reduction of aromatic carbonyl compounds to respective alcohols using different vegetables/fruits as biocatalysts

Plant/ vegetables common name	Scientific name	Substrate	Conversion (%)	Isolated yield (%)	ee (%)	References
Garlic	*Allium sativum*		95%	65%	90%	(Bilal *et al.*, 2019a)
			93%	70%	86%	
Mandarin	*Citrus reticulata*		-	49%	93%	(Bennamane *et al.*, 2018)
Strawberry	*Arbutus andrachne*		-	36%	95%	
Ginger	*Zingiber officinale*		-	40%	83%	
Artichoke	*Cynara scolumus L*		38%	43%	82%	(Nedjimi, Sekhri, 2016)
Dessert truffles	*Terfezia sp*		50%	16%	50%	
Date palm	Phoenix dactylifer L.		45%	69%	89%	
Coconut water	*Cocos nucifera L*		-	79%	95%	(Fonseca *et al.*, 2009)

HPLC using a UV detector at 210 nm. The structures were determined by IR spectra, ^{13}C NMR and ^{1}H NMR studies. The dehydrogenase enzyme present in *Daucus carota* could have reduced the compounds predominantly to (*S)* - alcohols with good yields of 60% - 95% and an ee of 76% - 99%. The pyridyls and pyrroles were reduced to form (*S)*-alcohols by following Prelog's rule while furan, thiophene containing ketones were reduced to (*R*) - alcohols with anti-Prelog's selectivity. In this study, 2-acetyl pyridine and 4-acetyl pyridine showed 100% conversion (Lakshmi, Reddy, Rao, 2011).

The aromatic homocyclic and heterocyclic aldehydes and ketones were reduced to their corresponding alcohol with excellent chemical yield using vegetables such as Broccoli (*B. oleracea var. italica*), spinach beet (*B. vulgaris var. cicla*),

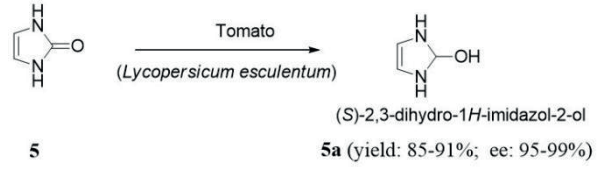


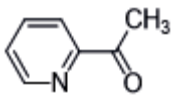
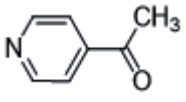
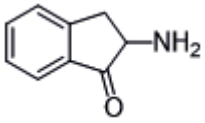
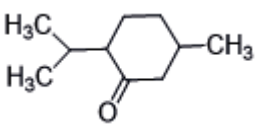
FIGURE 5 - Asymmetric reduction of imidazol-2-ones using tomato.

cauliflower (*B. oleracea var. botrytis*) and spinach (*Spinacia oleraceae*) as biocatalysts. The products thus obtained were analysed by GC-MS. Among these the *B. oleracea var. italic* and *B. oleracea var. botrytis* showed a maximum bioconversion yield of ≥99% in short reaction times (Suárez-Franco *et al.*, 2010).

The heteroaryl methyl ketones of pyridine and thiophene class compounds were reduced to corresponding (*S)* - alcohols using *Daucus carota* with a good to excellent ee of 93 - 98%. The reactive products were analysed by NMR spectral (^{1}H and ^{13}C) studies and the ee was determined using chiral GC and configuration was determined using polarimeter. It was evident from the study that compared to other vegetables, the *D. carota* showed a maximum yield and a better ee in reducing heteroaryl compounds (Aldabalde *et al.*, 2007).

In the reduction process of tetralone, 2-amino indanone and hydroxyl trimonoterpene ketones with *Daucus carota* plant to their respective chiral (*S*)-alcohols, were discussed. The reaction products were analysed using TLC, GC-MS, proton NMR, ^{13}C NMR, Infrared and Mass spectral studies. The substituted 1-amino-2-indanol from substituted 1-oximino indanones were carried out using *D. carota* with excellent yield, diastereoselectivity and enantiomeric excess. The products thus obtained showed preference for (*S*)-configuration, with a yield ranging from 80% - 90%, and diastereomeric purity of

TABLE III - Summary of reduction of homocyclic and heterocyclic carbonyl compounds to alcohols using carrot as biocatalyst

Plant/ vegetables common name	Botanical name	Substrate	Conversion (%)	Isolated yield (%)	ee (%)	References
Carrot	*Daucus carota*		100	95	99	(Lakshmi, Reddy, Rao, 2011)
			100	94	92	
			95	80-90	99	(Yadav *et al.*, 2007)
			70	80-90	99	

more than 95–98%. The enantioselective reduction of substituted 2-tetralones were studied using *D. carota* and the products thus obtained showed good yield (50–60%) and an ee (70–80%). Biotransformation of monoterpene ketones like menthone was reduced to the corresponding alcohols and the results stated that the *D. carota* enzymes reduced both carbon double bonds and the carbonyl group in the terpenoids. Thus, the enzyme present in *D. carota* showed a broad specificity, good yields of 80–90% and an ee of 88–99% (Yadav *et al.*, 2007). The bioreduction of homocyclic and heterocyclic carbonyl compounds to their respective alcohols using carrot are shown in Table III.

CONCLUSION

Biocatalysis is an effective way to reduce carbonyl compounds to their respective alcohols. Biocatalysts have been recognized and widely used in the production of a variety of optically pure chiral synthons for many years. In recent times, the use of plants as biocatalysts is increasingly gaining importance as they contribute towards sustainability and environmental protection. More importantly, the use of vegetables is more advantageous as they are cost effective, handling of vegetables is much easier than any other microbial biocatalyst as they do not require strict aseptic conditions and also they do not cause any opportunistic infections. Notably, the natural cofactor regeneration is confined within the whole cells itself and hence do not require any external addition of the same. With the help of plant tissues, a number of compounds with high efficiency and selectivity has been explored and characterized. On the other hand, plant cells exhibit only a narrow range of enzymes and the scope of doubling in undifferentiated cells is quite longer than microbial cells. As a result, the desired enzymes are often produced in very less quantities. The scientific advances reveal that different plant tissues from different sources may exhibit different catalytic characteristics. With this perspective, the present review compiles the use of different plant cells for the bioreduction of different carbonyl compounds towards the production of industrially/pharmaceutically important primary/optically pure secondary alcohols. Further, the use of plant cells as biocatalysts can be used for multi-enzyme cascade reactions and also can be scaled up for industrial processes.

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DATA AVAILABILITY STATEMENT

Data openly available in a public repository (Scifinder, PUBMED, Google Scholar).

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