Green and Environmentally Benign Organic Synthesis by Using Fruit Juice as Biocatalyst:  
A Review

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ABSTRACT

Facile and green synthetic approaches are important issues in organic synthesis. Green chemistry has become a motivational and inspirational tool for organic chemists to develop mild and benign pathways for the synthesis of biologically active compounds. The naturally available fruit juice as a biocatalyst in synthesis fulfills almost all the terms and conditions of green chemistry and attracted the interest of researchers. The best thing is that most of fruits are easily available, cheap and can be easily extracted. The purpose of this review is to look out present aspects of fruit juice in organic transformations.

 Keywords: Fruit juice; eco-friendly; biocatalyst; organic synthesis.
1. INTRODUCTION

With the start of twenty-first century, the public is much more aware of the hazardous substances used and produced during the chemical reactions, and hence the ‘concept of green and sustainable chemistry’ has been evolved. The main aim of this concept is to develop the smooth and nonpolluting pathways and to find creative ways to reduce the use of toxic reagents, solvents, harsh reaction conditions and expensive catalysts [1-3]. The experimental trials of new catalyst in an environmentally benign manner have become much more important in recent years [4]. The conventional synthesis of chemicals produces large amount of toxic wastes and by-products [5]. These threats indicate that it must be important to develop methods which satisfy green principles [6-7]. Among various green chemistry aspects, selection of catalysts for mild running of chemical reaction with optimum yield is most important part of the reaction procedure. Fruit juice plays an important role as a biocatalyst in many of the chemical reactions and this biocatalyst follows all the parameters of green chemistry. The multi-component reactions are the most important tools in organic transformations and pharmaceuticals. The concept of “Green Chemistry” has been widely accepted to complete the basic scientific challenges of protecting human health and environment [8]. In order to complete these needs, chemical reactions are proceeds in solvent-free [9-10], water as a solvent [11], ionic liquids [12], bio-based chemicals [13] and supercritical fluids [14] as green solvents. The increasing interest in fruit juice because these are available at low cost and non-toxic agents that can carry out an organic transformation in an environmentally benign manner. Fruit juice acts as homogenous catalyst for various organic reactions in easy and smooth way. The main motive of the present review is to represent the environmentally healthy use of fruit juice in organic transformations.

2. FRUIT JUICE AS A BIOCATALYST IN ORGANIC SYNTHESIS

2.1 The multi-component synthesis of substituted -2H-1,2,3-triazoles derivatives using lemon juice in ethanol by the reaction of 4-chloro-2-nitro aniline and 4-methoxy aldehyde with thiosemicarbazide in maximum yield [15]. They found that lemon juice plays a role of biocatalyst which provides non hazardous and mild conditions which are basic principles of green chemistry (Scheme-1).

2.2 Dihydropyrimidinone has been synthesized by reacting aldehydes, 1,3-dicarbonyl compounds with urea at room temperature under solvent free conditions [16]. This is a one-pot multi-component system reaction where lemon juice or pineapple acts as a green catalyst (Scheme - 2).

2.3 The synthesis of Schiff Base by using lemon juice (Citrus limonium) as an effective and mild acid catalyst for condensation reaction [17]. This synthesis shows the formation of selective imine by the reaction of aryl aldehyde and aromatic primary amine. This method provides a cost effective idea and benefits from the elimination of production of acidic waste (Scheme - 3).

2.4 A green procedure for Knoevenagel condensation was reported [18]. They showed that lemon juice (Citrus limonium) act as environmentally benign acid catalyst for the reaction between aldehydes and malononitriles. The mixture was stirred at room temperature for 30-120 minutes. This is new procedure by lemon juice qualifying it is a green method (Scheme - 4).

\[
\begin{align*}
\text{NH}_2 & \quad \text{CHO} & \quad \text{H}_2\text{N}-\text{S}-\text{NH}_2 \\
\text{Cl} & \quad \text{OCH}_3 & \\
R= \text{OH, OCH}_3, \text{CH}_3, \text{Cl}
\end{align*}
\]

Scheme – 1
2.5 The biocondensation of indoles and aldehydes for the synthesis of bis-, and tris (indoyl) methanes [19]. This reaction proceeds at room temperature for 5-6 hour. This method is suitable in term of short reaction time, reaction procedure is very simple and attained better yield of product (Scheme - 5).
2.6 Ecofriendly and clean one-pot synthesis of 3,4-dihydro-2(1H)-quinoxalinones and 3,4-dihydro-1,4-benzoxazine-2-ones [20]. Lemon juice (Citrus limonion) acts as an alternative to toxic solvents and catalysts. This reaction proceeds by substituted ester keto ester and substituted amines with lemon juice and reflux for 24h. After simple work up the newly synthesized products were isolated (Scheme - 6).

2.7 Green and economic method for the synthesis of benzopyran synthesis by using lemon juice (Citrus limonion) act as acid catalyst for cyclocondensation of salicylaldehyde and cyclic 1,3-diketones for benzopyran formation (Scheme- 7) [21].

2.8 The multi-component synthesis of substituted benzthiazole and benzoxazole derivatives using lemon juice in water by the reaction of 2-aminothiophenol or 2-amonophenol, aryl aldehyde and lemon water mixture (1:1) was added in reaction vessel [22]. They found that lemon juice plays a role of biocatalyst which provides non hazardous and mild conditions which are basic principle of green chemistry (Scheme-8).
2.9 An efficient and greener approach has been developed for the synthesis of 6-arylamino-5-cyano-2,3-dihydro-1,3-thiazin-4(1H)-ones, using Lemon juice (*Citrus limonium*) as a natural catalyst [23]. It was prepared via condensation of 3-arylamino-2-cyano-3-mercaptoacrylamides with several of aldehydes. The reaction proceeded in ecofriendly manner with excellent yields (Scheme-9). Most of the synthesized compounds were represents effective promising antimicrobial activity.

2.10 The acetylation of different amines and salicylic acid by using lemon juice (*Citrus limonium*) and acetic anhydride as an acetylating agent [24]. This reaction proceeds under normal reaction condition with formation of product in high yield. This method reduce the chemical wastage and more convenient than other reported methods (Scheme - 10).

2.11 A lemon juice catalysed ultrasound assisted, ecofriendly synthesis of schiff’s base [25]. A mixture of o-benzoic acid and 4-hydroxy-3-methoxy benzaldehyde was taken in sonication flask and then 2ml lemon juice was added drop wise under sonication probe (ACE probe, 20 KHz) at 40% amplitude for 2min. After complete addition of lemon juice, the reaction mixture was again exposed to acoustic cavitation for further 10 min, by keeping all the parameter constant. The completion of reaction was measured by TLC. The recrystallization was done by ethanol and a white solid pure product was obtained (Scheme - 11).

2.12 Tamarind (*Tamarindus indica*) fruit act as a biocatalyst for synthesis of bis-, and tris (indoyl) methanes and tetraindolyl compounds [19]. Excellent yield of product have been obtained by reaction of indoles with aldehydes by using microwave irradiation under solvent free conditions (Scheme - 12).

2.13 The synthesized the dihydropyrimidinone derivatives by reacting between aldehyde, ethylacetoacetate, urea/thiourea and 1ml tamarind juice (*Tamarindus indica*) was irradiated in an ultrasound at 100W for few minutes [26]. Microwave synthesis shows advantage over conventional heating by time, extent of chemicals used and by yield (Scheme - 13).

![Scheme-9](image)

![Scheme-10](image)

![Scheme-11](image)
2.14 The green synthesis of Schiff bases with grape juice (*Vitis Linata*), sweet lemon juice (*Citrus Limetta*) and extract of unripe mango (*Mangifera indica*) under solvent free conditions [27]. This reaction proceeds by stirring method, when the equimolar amount of benzaldehyde and aniline was taken in different beakers. In those reaction mixtures natural acid catalyst i.e. grapes juice were added in variable amounts (0.5 ml, 1 ml, 1.5 ml, 2.0 ml, 2.5 ml) and then kept for 5-10 minutes. Further each reaction mixture was stirred for 2 - 4 minutes at room temperature pale yellow solid crude product was appear after completion of reaction which was washed with distilled water and purified by recrystallization with minimum amount of ethanol. The same procedure is repeated with sweet lemon juice and aqueous extract of mango (Scheme - 14).

2.15 An ecofriendly and cost effective protocol for the synthesis of acetanilide by reacting aromatic primary amines and acetic anhydride, catalysed by aqueous extract of pods of *acacia concinna* fruit as a green catalyst [28]. This catalyst shows highly acidic nature (pH 2.1) and high solubility of reactant by hydrogen bond formation in aqueous solution. This type of unique protocol shows the economic and green pathways (Scheme - 15).

<table>
<thead>
<tr>
<th>Scheme – 12</th>
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<td>R= H, Me</td>
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<th>Scheme – 13</th>
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<tr>
<td>R= Ph, Ph-OMe, Ph-OH, Ph-NO₂, Ph-Cl, R₁= OEt</td>
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<th>Scheme – 14</th>
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<tr>
<td>1. Grape juice/ stirr for 5min</td>
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<tr>
<td>2. Sweet lime juice/ stirr for 5min</td>
</tr>
<tr>
<td>3. aq. extract of unripe mango/ stirr for 10-15min</td>
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</table>
2.16 An aqueous extract of *Acacia concinna* pods has been reported as a biocatalyst for Knoevenagel Condensation [29]. A equimolar mixture of salicylaldehyde and malonic ester and aqueous extract of *Acacia concinna* were taken in a round bottom flask and heated along with stirring at boiling water bath for 2h. After completion of the reaction, the reaction mixture as cooled at room temperature, the solid product was filtered off and recrystallized to get pure product (Scheme - 16).

2.17 The aqueous extract of the pericarp of *Sapindus trifoliatus* acts as a biocatalyst in the synthesis of al-damines in a chemoselective manner [30]. This reaction occurs by stirring the mixture of aromatic aldehydes and aromatic amines in presence of this fruit extract (Scheme - 17). This method provides a valuable reaction pathway against conventional method.

2.18 Most sustainable reduction of aliphatic and aromatic aldehydes and ketones by using fresh coconut juice (*Cocos nucifera*) as a biocatalyst [31]. Thus, when the various carbonyl compounds were treated with freshly prepared coconut and the mixture was shaken at room temperature for 72 h, produced alcohols (Scheme – 18a), (Scheme – 18b), (Scheme – 18c), (Scheme – 18d). Fonseca and co-workers also reported the hydrolysis of ester (Scheme – 19a), amide (Scheme – 19b) and anilides (Scheme – 19c) by using coconut juice. This bioconversion provides a significant role of green chemistry.
2.19 A new greener alternative for bioreduction of aromatic aldehydes (Scheme – 20a) and decarboxylation of substituted aromatic acids (Scheme – 20b) using coconut water as a biocatalyst [32]. This is an effort towards the energy efficient, eco-friendly transformation of interesting organic molecule.
HORH ORH Ar

2.20 The synthesis of vanillin derivative using coconut water as a green catalyst [33]. Thus, when equimolar amount of vaniline, ethylacetoacetate, thiourea and 5ml coconut water and carried out the reaction in microwave for 120 seconds by using minimum power 180 watts. After a simple work up and recrystalization is done by proper solvent, the pure product with a good yield was obtained (Scheme – 21). This method is very simple, economical, mild and environmentally benign as compared to classical reactions.

2.21 The synthesis of aryldiene malononitrile by Knoevenagel condensation reaction of aldehydes and malononitrile under visible light produced by tungsten bulb [34]. Aqueous extract of keora fruit can catalyze the Knoevenenagel condensation with a good yield of products. Aqueous extract of keora is acidic and hence it could be work as acid catalyst for reaction (Scheme-22).

2.22 A mild and environmentally benign synthesis of 3,4,5- substituted furan-2(5)-ones employing aqueous extract of seedless barberry (Berberis integririma) as a biocatalyst [35]. The equimolar amount of substituted aldehyde, substituted amine and dialkylacetylene dicarboxylate and 5ml of barberry juice were stirred at room temperature. This method prevents the generation of waste rather than the conventional chemical reagent (Scheme-23).
2.23 An efficient multicomponent synthesis of 3,4,5- substituted Furan-2(5h)-ones catalysed by watermelon juice [36]. The equimolar amount of substituted aldehyde, substituted amine and dialkylacetylene dicarboxylate and 5ml of watermelon juice of watermelon were stirred at room temperature. The completion of reaction was checked by TLC, after that the reaction products were collected by filtration. Thus, the products were washed with water/ethanol (50:50) to give the pure compound. The catalyst remained in the water/ethanol filtrate (Scheme 24).

2.24 A simplified green chemistry approaches in organic transformation [37]. Grape fruit which is an efficient and mild biocatalyst for some selected organic reactions in solvent-free conditions. This catalyst is stereoselective in the biotransformation of chloro-polycyclic aromatic compounds (Scheme – 25).

2.25 Assymmetric reduction of Ketones by using Tomato juice (Lycopersicumesculentum) as a biocatalyst [38]. Thus, this reaction provides a biocatalytic preparative method of asymmetric alcohols (Scheme – 26a), (Scheme – 26b) and (Scheme – 26c). This technique is more ecofriendly and provides an important approach towards green chemistry.

2.26 Fast microwave assisted bioreduction of aromatic and aliphatic aldehydes and ketones by using Aloe vera juice (Scheme - 27) [39]. Microwave-assisted synthesis was used in the biotransformation of these organic compounds which acts as a very useful intermediate in various organic reactions. This simple, efficient and ecofriendly method.
2.27 The synthesis of Dihydropyrimidinone (DHPM) derivatives via one-pot multicomponent cyclocondensation namely Biginelli reaction employing urea, ethylacetoacetate with a series of different derivatives of benzaldehyde in fruit juice (viz. orange juice, lime juice, amla juice) at room temperature (Scheme-28) [40]. They found that all the fruit juices are totally non-polluting, inexpensive and 100% biodegradable.

2.28 A great contribution to the green chemistry by using crop-derived products, like juices obtained from edible fruits and vegetables and waste waters deriving from agriculture and industrial processing. They described the juices waste water promoted synthesis of coumarin-3-carboxylic acid (Scheme-29), and synthesis of cinnamic acids (Scheme-30) with high purity [41]. The Knoevenagel condensation have been accomplished by using substituted aldehyde and meldrum's acid as substrates, both are mixed in the aqueous medium represented by lemon, grapefruit, carrot, pomegranate, kiwi, vinegar, tomato and buttermilk waste water. The process was carried out for 24h under magnetic stirring at room temperature. Pure product have been isolated as solids after filtration in very good yields and the biocatalysts were recovered after filtration from all reaction media reused without any loss of activity.

\[
\begin{align*}
\text{Scheme-29} & \quad \text{Ar} = \text{Ph-CH}_3, \text{Ph-Cl}, \text{Ph-OCH}_3 \\
\end{align*}
\]
Table 1.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Carbonyl Compounds</th>
<th>Product (Scheme-29)</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
<th>I</th>
<th>J</th>
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<tbody>
<tr>
<td>1</td>
<td>Salicyladehyde</td>
<td>R²=R³=R⁴=R⁵=H</td>
<td>99</td>
<td>96</td>
<td>97</td>
<td>96</td>
<td>95</td>
<td>95</td>
<td>92</td>
<td>94</td>
<td>99</td>
<td></td>
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<tr>
<td>2</td>
<td>4-(Dimethylamino) salicyladehyde</td>
<td>R²=R³=R⁴=H, R⁵=N(Et)₂</td>
<td>99</td>
<td>99</td>
<td>92</td>
<td>93</td>
<td>94</td>
<td>96</td>
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<td>97</td>
<td>91</td>
<td>96</td>
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<tr>
<td>3</td>
<td>4-nitrosalicylaldehyde</td>
<td>R²=R³=R⁴=H, R⁵=NO₂</td>
<td>98</td>
<td>97</td>
<td>97</td>
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<td>4</td>
<td>5-bromosalicylaldehyde</td>
<td>R²=R³=R⁴=H, R⁵=Br</td>
<td>99</td>
<td>97</td>
<td>99</td>
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<tr>
<td>5</td>
<td>2,4-dihydroxybenzaldehyde</td>
<td>R²=R³=R⁴=H, R⁵=OH</td>
<td>97</td>
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<td>95</td>
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<tr>
<td>6</td>
<td>2-hydroxy-5-nitroacetophenone</td>
<td>R²=Me, R³=NO₂</td>
<td>96</td>
<td>95</td>
<td>98</td>
<td>98</td>
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<tr>
<td>7</td>
<td>5-chloro-2-hydroxyacetophenone</td>
<td>R²=Me, R³=Cl</td>
<td>98</td>
<td>97</td>
<td>99</td>
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<td>2-hydroxy-4-methoxyacetophenone</td>
<td>R²=Me, R³=OMe</td>
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<td>9</td>
<td>2,5-dihydroxyacetophenone</td>
<td>R²=Me, R³=OH</td>
<td>94</td>
<td>94</td>
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<td>11</td>
<td>2-Hydroxyacetophenone</td>
<td>R²=Me, R³=OH</td>
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A= lemon juice, B= grapefruit juice, C= carrot juice, D= pomegranate juice, E= kiwi juice, F= vinegar, G= tomato juice, H= limencello, I= olive mill waste water, J= buttermilk, %Y= Percentage Yield
**Table 2.**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Carbonyl Compounds</th>
<th>Product (Scheme-30)</th>
<th>A %Y</th>
<th>B %Y</th>
<th>C %Y</th>
<th>D %Y</th>
<th>E %Y</th>
<th>F %Y</th>
<th>G %Y</th>
<th>H %Y</th>
<th>I %Y</th>
<th>J %Y</th>
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<tr>
<td>1</td>
<td>Benzaldehyde</td>
<td>R¹=R²=H</td>
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<td>96</td>
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<tr>
<td>2</td>
<td>Vanillin</td>
<td>R¹=OH, R²=OCH₃</td>
<td>95</td>
<td>92</td>
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<td>3</td>
<td>p-hydroxybenzaldehyde</td>
<td>R¹=OH, R²=H</td>
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<td>p-floro-benzaldehyde</td>
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<td>R¹=Cl, R²=H</td>
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<tr>
<td>11</td>
<td>4(3,3,Dimethylallyloxy)-3methoxybenzaldehyde</td>
<td>R¹=3.3,Dimethylallyloxy, R²=OCH₃</td>
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3. CONCLUSION

Natural juices contain various acids act as natural acid catalyst in organic synthesis. These reactions were carried out at room temperature and under solvent free conditions. This review study provides an alternative for harmful catalysts for organic synthesis. These biocatalyst does not harm to environment and economic in nature. This article is dedicated to green chemistry and an attempt to suggest ‘Go Green’ for all academic and industrial researchers.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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