Green synthesis of Schiff bases: a review study

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ABSTRACT

Objectives: Green chemistry is the field that implies instruments and procedures, by which it offers significant environmental and financial benefits above traditional synthetic methods. The modern attention in green chemistry has pretended an additional need for organic synthesis in which different reaction environments must locate, which decreases the use of toxic organic solvents or toxic chemicals. These green methods must enhance the selectivity, shorten reaction time, and make the products isolation simpler than the ordinary routes. In the 19th century, Hugo Schiff recorded the first synthesis of Schiff bases (imines). A Schiff base is considered as an aldehyde with a C=N group (azomethine group) instead of the C=O group. It is normally produced by condensation of primary amines with aldehydes. Schiff bases entertain many important biologically and pharmaceutical activities and they are distinguished for their pharmacological action and wide-range applications in the food industry.

This study tries to focus on the green synthetic methods used for Schiff bases synthesis, in order to find the best technique that offers higher yields in shorter time within eco-friendly environment.

Conclusions: The review considered many green synthetics techniques, from which the microwaves irradiation method is considered to be the best followed by the ultrasonic, natural acids utilizing and grinding methods.

Keywords: Green chemistry, Green synthesis, Schiff base, eco-friendly environment

مجال البحث: الكيمياء الخضراء هي المجال الذي يتضمن الإجراءات والأدوية التي تقدم فوائد بيئية ومالية وصحية مقارنة بطرق التصنيع التقليدية. لقد ازداد الاهتمام جدًا بالكيمياء الخضراء نظرًا للحاجة المتزايدة لتصنيع المركبات العضوية والذين يتم ضمن بيئات تفاعل مختلفة. وذلك من أجل التقليل من استخدام المذيبات العضوية أو المواد الكيميائية السامة. اساليب الكيمياء الخضراء متعددة ومنها تقصير وقت التفاعل أو جعل نواتج التفاعل أكثر سهولة.

سجل العالم هو عالم في القرن التاسع عشر. حيث تعتبر قواعد شيف ببساطة عالم أليهاند مع استبدال مجموعة الكاربون بمجموعة الأروماتين، ويتم إنتاجها عادةً عن طريق تكثيف الأمينات الأولية مع الألدهيدات. تستعمل قواعد شيف في العديد من الأنشطة البيولوجية والصيدلانية المهمة وتعزز بتأثيرها الدوائي وتطبيقها الواصفة النطاق في صناعة الأغذية.

تحاول هذه الدراسة التركيز على جميع طرق التصنيع الخضراء المستخدمة في تحضير قواعد شيف، من أجل إيجاد أفضل تقنية تقدم أعلى نتائج في وقت قصير وضمن محيط صديق للبيئة.

الاستنتاجات: تناولت هذه الدراسة العديد من تقنيات الكيمياء الخضراء، بينت النتائج أن طريقة الساكروريث هي الأفضل تليها طريقة الأحماض الطبيعية وثم طريقة الفوق الصوتية وطريقة الطحن.
INTRODUCTION

Green chemistry is a recent path for examining the organic synthesis and the drug design methodology [1]. It is that section of chemistry involving apparatuses, procedures and tools, in which significant environmental and economic benefits above conventional synthetic processes offered [2]. The current attention in green chemistry has postured many encounters for organic synthesis from which a modern reaction environments need to be created that involves decreasing the use of organic solvents or the utilization of toxic chemicals [2,3]. Many procedures utilizes by the green chemist involving solvent free reactions, simplifying the workup procedures, minimizing reaction time, enhanced selectivity and simplify purifications procedures compared to the traditional methods [4].

Hugo Schiff recorded the first synthesis of Schiff bases (imines) in the 19th century. A Schiff base is considered as an aldehyde bearing a C=N group (azomethine -N=CH- group) in stead of the C=O group [5,6]. It is usually formed from the reaction of aldehydes with primary amines [7,8]. The standard Schiff bases chemical expression is $RCH=NR_1(R \& R_1$ characterizes alkyl or aryl substituents) [9, 10].

The Schiff bases synthesis is regularly done by nucleophilic addition of the NH$_2$ group to the C=O of the aldehyde forming a hemiaminal compound in azeotropic reflexing condition with the concurrent elimination of water, which then dehydrated to generate an imine [11] as shown in the following equation [12]:

\[
\begin{align*}
&\text{R}_1^\text{CH} \equiv \text{N}^\text{R}_1 + \text{R}_2^\text{R}_3^\text{NH}_2 \\
\rightarrow \quad &\text{R}_1^\text{CH}^\equiv \text{N}^\text{R}_1 + \text{H}_2\text{O}
\end{align*}
\]

Applications of Schiff base:

Schiff bases are well-known as pharmacologically active compounds and have wide-range utilizations in food manufacturing [13], colors and dye manufacturing, analytical and medical chemistry, and also in synthetic chemistry [6,8,14]. They are also utilized as ligands in metal ions complexes formation, and also as stabilizers in polymers synthesis [14,15].

Schiff bases provide many important biological activities like antituberculosis, antifungal, antimalarial, antibacterial, anthelmintic, anti-HIV, diuretic, anti-inflammatory, antiviral, antitumor, antiprotozoal, anticonvulsant, and analgesic activities [13,16-20].

Thus, the importance of Schiff bases is significantly clear. This study aimed to concentrate on the green synthetic routes used for Schiff bases synthesis, to characterize the best technique that offers higher yields in a shorter time within the ecofriendly environment.

Conventional method for the synthesis of Schiff bases

Schiff base synthesis frequently performed by refluxing a mixture containing equimolar of primary amines and aldehyde within non-aqueous organic solvents for 8-12 hours. The reaction is acid catalyzed and usually proceeded with an azeotroping agent (if necessary), or by separating the formed water [9,17,18]. This reaction is considerably reversible and it is
beneficial to eradicate the produced water away from the reaction to acquire a maximum yield of the Schiff bases [21,22].

Green synthetic methods for Schiff bases synthesis

1-Microwave irradiation method:

Microwave supported organic reactions have appeared as a modern appliance in the synthesis of organic compounds. Significant benefits of this technique involve extremely accelerate reaction rate, therefore minimizing reaction period beside an enhancement in the yield and product quality and simpler procedure compared to traditional methods [18]. Moreover, this method is respected as a valuable policy under “Green Chemistry” for its environmentally-friendly properties. The implication of microwave in organic synthesis has ascertained to be effective, harmless and environmentally gentle procedures with the quicker time needed to perform the reaction [23,24].

Currently drug companies are utilizing microwaves in the zone of organic/ pharmaceutical manufacturing [25]. Microwave assisted reactions (solvent or solvent free environments) have acquired acceptance because of quicker reaction rates, a cleaner environment and simplicity of operation. [26]

In 2015, Bhusnure et al. dedicate the synthesis of Schiff bases as promising antimicrobial agents [18]. They utilize the 2-ethoxyethanol as a wetting reagent and the source of heating as microwave irradiation. The aldehydes and the amines mixed with two drops of β-ethoxyethanol in a beaker. The reaction mixture was microwaved at (180W-600W) for about 3 minutes (giving a short interval of cooling), the best microwave situations were among 180 - 360W microwave power [18]. This straightforward microwave technique presents several Schiff bases with rapid reaction times, exceptional yields and without the development of unwanted side products. They found that this method was an extra effect on the whole operation compared to the typical methods.

Seewan and coworkers (2018) synthesized a group of imines by the reaction of 4-aminoantipyrine with various substituted aldehyde, both dissolved in absolute ethanol. The mixture irradiated in a microwave oven for 1 minute at 300W. They indicated the efficacious technique of synthesizing by microwave irradiation with 97% yields [27].

Pooja et al.(2014) designated a new group of Schiff bases by utilizing glucose to act as a catalyst in the reaction of p-toluidine and various aromatic aldehydes in water. All the reactions done under microwave irradiations [28]. Glucose being absolutely harmless, biodegradable, inexpensive and environmentally nontoxic has enormous potentiality to be used as ecofriendly catalyst. P-toluidine and requested aldehyde mixed with 10 ml of glucose solution. The reaction mixture irradiated MW at (240 W) for the specified time. The products acquired in excellent yields [28].

Recently Tapabashi et al. (2021) Synthesize a set of Schiff bases by irradiating the reaction mixture for 15 - 20 minutes, in a microwave reactor at moderate to high temperature after addition (3 - 4) drops of DMF. The same
procedure applied by replacing DMF with (6 - 8) drops of glacial acetic acid. Both methods give reasonable to good yield and in a short reaction time [29].

2-Natural acid-catalyzed methods

The increasing attention about the natural acid catalyst (as fruit juice) in chemical synthesis is principally belong to their acidic nature, benign environmental character, enzymatic action and low-cost. There are now concentrating on the significance of fruit juice as a natural biocatalyst in organic synthesis [30]. The natural acid (for example the lemon juice) offers moderate acidity that helps to catalyze the reaction at 25º C. Recently fruit juices recognized as possible organic solvents for the synthesis of pharmaceutical compounds [2, 30].

Yadav and coworkers (2015) with aid of sweet lemon or grapes juice or aq. extract of unripe mango (as catalytic solvent), they synthesized a group of Schiff bases by stirring method. The equimolar amount of benzaldehyde and aniline mixed, and the natural acid catalyst (0.5- 2.5 ml) added and the mixture preserved for 5-10 minutes [2]. Moreover, the reaction mixture stirred for 2-4 min. at 25º C. They mention that the heteroatom protonation that occurs in molecular conversion done by the aid of natural acids. All these natural juices restrain various organic acids like malic acid, tartaric acid, citric acid, oxalic acid. These acids are offer the required pH to catalyze the synthesis of Schiff bases [2].

Desai and Shinde (2015) proposed a conventional procedure for the green synthesis of nicotinic acid hydrazide Schiff base [31]. Nicotinic acid hydrazide dissolved in ethanol and lemon juice added to it with stirring, then the aldehydes added with stirring at room temperature for 15 minutes. They developed an original, straightforward and environmentally gentle synthesis of nicotinic acid hydrazide Schiff bases in beneficial yields [31].

Jadhao and coworkers (2016) make use of an original green route for the development of Schiff bases utilizing Natural acid catalyst (lemon juice) [30]. First, a precursor made from Acetophenone and semicarbazide hydrochloride synthesized. Then this precursor added to alcoholic solution of several aldehydes using lemon juice as catalyst. They refluxed the reaction mixture at 25º C for 1.5 hour. Their results show that the natural acid provide a suitable acidic medium to perform the reaction in good yields. The method was clean, safe and environment-friendly [30].

3- Ultrasonic methods:

Sonication is the employing of sound power to excite particles for deferent principles. Ultrasonic in frequency (>20 kHz) are typically used by a process recognized as ultrasonication [16, 32]. In the laboratory, it is usually employed by utilizing an ultrasonic bath or probe, this instrument identified as a sonicator [32].

Thalla et al. (2012) proposed a new method for the nicotinohydrazone Schiff bases synthesis under catalyst-free ultrasonic irradiation conditions. In this distinctive synthetic procedure, nicotinohydrazide and m-nitro benzaldehyde in 15 mL of water exposed to ultrasonic irradiation at 60 ºC for 14 min to afford 92% yield as compared to 84% yield by ordinary method [16]. They developed an effective and
ecofriendly approach for Schiff base synthesis to present optimum yields in an aqueous medium employing ultrasonic irradiation environments without using any catalyst [16].

In another study, Nikpassand et al. (2013) established an effective, green, rapid and accessible technique for the azo-linked Schiff bases synthesis by the reaction of azo-linked aldehydes and aminopyrazole under ultrasound irradiation [32]. This method propose benefits such as minimizing reaction time, mild condition and higher yields. They made a mixture of azo-linked aldehydes and aminopyrazole in 10 mL ethanol, and then they irradiated the mixture in a water bath by (45 kHz) ultrasound at 60°C for (5-15min). The pure products collected in 85-96% yields. They conducted that the higher yield and less reaction time by ultrasonic method attributed to the developed bubbles burst, which develops elevated temperature and pressure that assist the intermolecular reaction [32].

4- Grinding method

In (2011) Zarei and Jarrahpour established appropriate, quick greenly methods for the Schiff bases synthesis with solvent and refluxing free condition, with excellent yields and rapid reactions [33]. The azo Schiff bases synthesis was performed by grinding the aldehyde with the amine in a mortar for one minute and then preserving the mixture at 25°C for 1.5 h. The yielded water was eliminated under vacuum at 70 °C. This method was fast and economic; the reactions progressed at room temperature with excellent yields, without the need for any base [33].

Sharma and Bhardwaj (2017) recorded the synthesis of Schiff bases by solvent free route utilizing the amino acids (Glycine, Phenylalanine and Tyrosine) and the salicylaldehyde [34]. The method involves solid-state synthesis by using pestle and mortar. The procedure is completely free of solvent. Equimolar quantities of reactants are mixed in a mortar and then grinded for 10 min. with a pestle. A yellow gum is formed which transforms to a solid powder on continuous grinding after 20-30 minutes. This method is recognized to be simple and can provide superior yield. The frictional heating resulting from the physical action of grinding on molecular crystals, push the reaction to the forward direction [34].

Sachdeva and Khaturia (2017) in their mini- review mentioned that Zarei et al. stated the synthesis of new Schiff bases in excessive quantities by grinding at 25°C [35]. Azo-aldehyde reacted with corresponding amines in minimum amount of water to generate azo Schiff bases in very good yields [36].

The green procedure which utilizing grinding of the reactants at room temperature, that yielded 90-95% was conducted by Meenakshisundaram and Manickam (2019). The simple reaction conditions, easy, harmless and clean procedure with good yields are the benefits of this novel method. The dialdehyde and their corresponding amines were added in a mortar and grinded for 10 min to get the Schiff base (yield 70-75%) as solid [37].

Hanadi (2020) synthesize new Schiff bases complexes by a green procedure, utilizing the ball-milling technique [38]. Also, ball milling was used by Alharbisia and his coworkers (2021) to acquire new Schiff-base
complexes from, Fe, Ni, Zn and Co ions, which categorize as a green pathway of synthesis [39].

5- Water as a green solvent

The use of water as a reaction medium offers several advantages as it is cheap, non-inflammable, non-toxic and safe to use [1,3, 41].

Rao et al. (2010) demonstrated the preparation of Schiff bases in an aqueous medium with good yields, which are higher than the ordinary methods. This technique has the benefit that it does need any acid catalysts. The yielded Schiff bases can be separated by filtration, and it is worthy to indicate that the reactions pressed in efficient manner by water [41]. This method accelerates the reaction rate by nearly 300-fold. The method involves the addition of salicylaldehyde to a solution of 1,2-diaminobenzene in 10 ml of water. The developing mixture was stirred for 10 min at 25 °C. The yield was 95% compared to 65% yield in the conventional method. This method is considered an appropriate, easy, effective, and environmentally-friendly green procedure for Schiff bases synthesis [41].

Another study by Bhat et al. (2017) demonstrates an appropriate, effective and environmentally-friendly method for synthesis of the Schiff base derivatives under mild conditions using water at room temperature [1]. They dissolve salicylaldehyde and ethylenediamine in water as a solvent and shake it to dissolve the components. Then they reflux the mixture for about 2.5 hours at 70°C [1].

In another study, the synthesis of salicylaldehyde-based Schiff bases was conducted by Shamly (2018). 3-amino benzoic acid, aniline, ethylene diamine in 10 ml of water mixed with salicylaldehyde [40,41]. Then the mixture was stirred at 25 ºC for 10 min to get the 83% yield. Here water plays the role of ecofriendly solvent [40].

6- Miscellaneous methods

A- Magnetic nanoparticles

Magnetic nanoparticles (MNPs) considered as fascinating and desirable stuffs due to their high surface area and exceptional magnetic characteristics [42]. Nezhad and Tahmasebi (2019) consume ionic liquid carried on magnetic nanoparticles as an effective and recyclable eco-friendly catalyst for benzimidazoles synthesis in solvent or solvent-free environments. A mixture of o-phenylenediamine and corresponding aldehyde was well-stirred with catalyst (Fe₃O₄ magnetic nanoparticles) in 10 mL of water, or under solvent-free conditions at 80 °C, both methods for 25-40 min. The benefits of this methods were its easiness procedure, minimum reaction times in comparison to the other procedures, and the good yields of products. In addition, the catalyst can be reused several times and recovered easily by simple magnetic decantation with no loss of activity [42].

B- Mixing at room temperature

While Ariyaefar and coworker (2018) synthesize a series of chiral Schiff base compounds by the addition of 3,5- dichlorosalicylaldehyde to an aqueous solution of (R)-3-Amino-1,2-propanediol at 25°C which yielded a yellow precipitate almost immediately [43].

C- Garlic as natural biocatalyst
Bedi and coworkers (2020) establish the use of natural biocatalyst (garlic) for eco-friendly synthesis for a group of Schiff bases, they utilizing p-toluidine and many aromatic aldehydes as reactants. The Schiff bases produced high yields by merely grinding the reactants collectively with a pestle in a mortar with the existence of a piece of garlic in solvent free procedure. Their method was very easy, eco-friendly, efficient, cost-effective it is within the green chemistry protocols [44].

7- Comparison studies

Yang and his coworkers (2006) compare three ways for the synthesis of simple Schiff bases: microwave method, reflux method and by utilizing anhydrous MgSO₄ [45]. In the microwave method, a mixture of p-toluidine, 3,4,5-trimethoxybenzaldehyde with neutral alumina in DCM (2ml) was presented in a microwave oven and irradiated for 4min (20% output power) and the yield was 85%. While in the second method a solution of the same reactants in (10ml) benzene was reflux until no water developed (observed by a Barrett distilling receiver), and the yield was 72%. In the third method: to a stirred solution of the same reactants in 10ml dichlorometham, anhydrous MgSO₄ was added. Then the resultant mixture stirred for 2 hours at 25°C and the yield was 75%. By comparison, the microwave method has a great advantage as it utilize minimum time with maximum yield [45].

Taj et al. (2011) synthesize Schiff bases in different conditions using sulphuric acid [46] and Lewis acids acid [47,48] as catalysts. In the method I: A mixture of the amines, aldehyde and conc. H₂SO₄ or glacial acetic (2 drops) in 5 ml alcohol refluxed for 4 h over water bath which results in poor yields (30%). In method II: A mixture of the same reactant in 5 ml DCE and magnesium perchlorate Mg(ClO₄)₂ was refluxed for 3 h intervals in the water bath. Mg(ClO₄)₂was separated by filtration. This method gives excellent yields (75%) [48].

In (2012) Sachdeva and his coworkers compared four different methods for Schiff bases synthesis. In the method I: the grindstone friction-activated synthesis was tested [49]. The same molar quantities of dl-alanine amino acid and corresponding aldehyde dissolved in a least amount of water. Then the mixture grounded for 5–10 min by a pestle in a mortar. The primary slurry mixture hardened through 20–25 min and then left overnight (8 h). In method II: stirring was tested by mixing an equimolar of the same reactants with 5 ml of water, then the mixture was magnetically stirred at (25°C) until the completion of the reaction. Method III involved reflexing the same reactants with 10 ml of water for 1 h. While in method IV: the microwave irradiation was tested as an equimolar mixture of the same reactants mixed with 5 ml of water and irradiated in a microwave oven at 250 W for 5–6 min. In this study, they try to synthesize Schiff bases using water as a green solvent. The results confirming that stirring at 25°C and microwave methods are easier and quicker than methods I and III. All the described methods are considered as eco-friendly techniques as they utilize no organic solvent[49].

Another comparison study made by Chawla et al. (2015) in which they synthesize a group of Schiff bases by different methods [50]. In the first one, they make use of glacial acetic acid as
catalyst and ethanol as solvent by reflexing equimolar quantities of 4-amino benzene sulfonamides with different aromatic aldehydes at 50-60°C. The second method involved microwave irradiation in an open vessel with or without organic solvents. It was found that the condensation reaction progress rapidly and efficiently without solvent, but it needed only 2–3 minutes if a catalytic amount of glacial acetic acid was used. The natural acid catalyst was the third method in which lemon juice (natural acid) in solvent-free conditions mixed with the reactants for 30 minutes, which afford the Schiff bases in excellent yields (94%). This green reaction has several eco-friendly benefits like minor reaction environments and easy work-up with elevated yield. The fourth method makes use of Lewis acids (ZnCl\textsubscript{2}, TiCl\textsubscript{4}, alumina and P\textsubscript{2}O\textsubscript{5}) in order to overcome the removal of water complications [50]. Lewis acid fastens nucleophilic attack of amines on carbonyl carbon in addition to serve as a drying agent for efficient water elimination in the second step. In the fifth method equimolar quantity of p-toluidine and vanillin mixed and preserved in U. V. compartment for 15 min, the yield was 96.90%, which is more than the traditional method (72-78%). While in the sixth method they utilize the sonicator with or without catalyst at 45°C for 13-15 min, the yield was found to be 97%. The catalyst acetic acid was reduce the time of the previous experiment to 9-10 min with the same yield. The last method was by utilizing mortar and pastel to mix equimoler quantity of p-toluidine and vanillin for 10-12 min, then the product was located in a dark room, overnight standing and the yield was 95.80%. At the final, they conclude that by comparing with the traditional method, these methods are more appropriate with higher yield in quicker time and simple conditions, with no pollution generation. The priority was with the microwave method [50].

In another study, Arafa and Shaker (2016) synthesized a group of new bis-Schiff bases under microwave irradiation, sonication and regular methods with no catalyst [51]. In the conventional method, salicylaldehyde derivatives and diamines suspended in ethanol, and then the mixture stirred for 10-12 h. The microwave method involved mixing the same reactants and irradiating them with 450 W for 6-10 min at 25°C. While in the ultrasonication method, the same reactants dissolved in ethanol (5 mL) and then occupied in an ultrasonic water bath at (25°C). Then subjected to ultrasound irradiation for 1-4 min. At the end, they observed that, the ultrasound method enhanced the yield and minimized the reaction rate. Nevertheless, the microwave irradiation show no valued enhancement in the yield (70-88%) even when they increase the irradiation times [51].

Kapadnis and his team (2016) tested four synthetic methods of Schiff base [52]. The microwave irradiation was the first one in which a few drops of 10% NaOH were added to reactants in order to adjust the pH. Then the reaction mixture irradiated for 8 min in the microwave oven. In the second method, they reflux the previous mixture for about 8 hrs. The stirring was the third method, the same previous mixture was stirred on a magnetic stirrer for 5 hrs. at room temp. The grinding was the last method in which the reactants mixed with 10ml ethanol in a mortar pestle, then a few drops of citric acid was added.
to adjust its pH with grinding for about 20 min. The results indicated that the first method has a great advantage. It is very appropriate for industrial manufacturing which utilizes a shorter time and also has the highest yield[52].

A review study made by Shntaif and Rashid (2016) mentions several methods for Schiff bases synthesis under microwave irradiation[53]. They either mixed the reactants with or without alcohol, or they added acetic acid with ethanol, or used glacial acetic acid as a catalyst with DMSO, or even they make use of neutral alumina, silica gel or concentrated sulphuric acid as catalysts. All these methods conducted under microwave irradiation. In the end, they conclude that these methods were valuable tools for minimizing reaction times and enhancing the yields[53].

Dayma et al. (2018) made a comparative study using various Schiff bases synthesis methods[54]. In the conventional method, 2-3 drops of acetic acid were added to a mixture of salicylaldehyde with sulphanilic acid in ethanol, and the resulting mixture stirred at ambient temperature for 4 hours. While in room temperature method, a solution of the same reactants in ethanol stirred by magnetic stirrer at (25º C) for one hour (few drops of acetic acid gradually added). While in the grindstone method, the reactants mixed with few drops of acetic acid and ground together in a mortar using a pestle to produce a yellow solid within 20-40 min. In the microwave method, the reactants dissolved in ethanol, and one drop of glacial acetic acid added, then the mixture irradiated in a microwave at (140 W) for 2-3 minutes. The best yields obtained in microwave method. The result also exposes that the grindstone method is superior to the ordinary method. No organic solvent needed, the reaction proceeded in relatively short with good yields[54].

A new series of Schiff bases as NO donor was synthesized by Sravanthi et al. (2019) using green methodology by condensation of 2-hydroxyacetophenone with Furfuryl amine via four methods[4]. An efficient, green, cheap and eco-friendly method via microwave-assisted reaction in fruit juice medium has developed. This method also compared with the conventional method, grinding method and ordinary microwave method. The Microwave method using fruit juices as catalyst evidence to be simple, effective and eco-friendly compared to other methods of synthesis[4].

An original synthetic method for imidazole Schiff bases conducted by Eftekhari et al. (2020)[55]. The synthesis involves heating, microwave irradiation, and with ethanol. The results indicated that Schiff bases were synthesized in microwave and ethanol methods were in maximum yields (90-98%), it takes only 2-4 min. The exceptional benefits of microwave irradiation include reducing the time of reaction from an hour to a minute and increasing the products yield[56].

Xochicale-Santana et al. (2021) reported the design, synthesis, and chemo-photophysical characterization of two Schiff bases derived from 4-aminobenzoic acid 4-(4-(diethylamino)benzylidene)aminobenzoic acid and 4-(4-methoxybenzylidene)aminobenzoic acid. However, the Schiff bases obtained with green synthetic techniques (ultrasound and mechanosynthesis)
minimize the time and energy needed comparing with traditional heating [57].

**CONCLUSION**

Green chemistry offers significant environmental and financial benefits above traditional synthetic methods. The green synthetic methods must enhance the selectivity, shorten reaction time, and make the purification of products simpler than the traditional methods. A Schiff bases formed by condensation of primary amines with aldehydes. This study focused on the green synthetic methods that are used for Schiff bases synthesis in order to find the best technique that offers higher yields in a shorter time in ecofriendly environment. The review considered many green synthetics techniques, from which the microwaves irradiation method considered the best followed by the ultrasonic, natural acids utilizing and grinding methods.

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