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Conversion of Jatropha Oil to Green Hydrocarbons through Decarboxylation Process over Mesohydrotalcite Catalyst

Hong Khanh Dieu Nguyen* **and Hung Van Nguyen**

Hanoi University of Science and Technology, No. 1, Dai Co Viet street,
Hai Ba Trung district, Hanoi City, **VIETNAM**
Email: dieuhong_bk@yahoo.com

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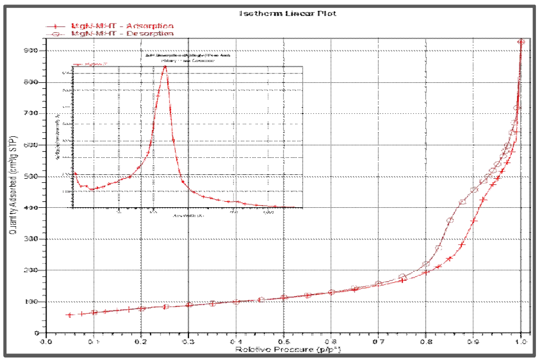
ABSTRACT

Vietnamese jatropha oil was converted to rich green hydrocarbon products under batch decarboxylation conditions using novel mesoporous Mg-Al-Co hydrotalcite based catalyst (mesohydrotalcite catalyst). The catalyst having pore width of 130Å was modified to other ones with pore width of 38Å by changing its preparation method from co-condensation-evaporation to hydrothermal treatment. The narrower pore width of the catalyst greatly contributed to its selectivity with free fatty acids in the decarboxylation process, which positively enhanced the hydrocarbon products. The decarboxylation parameters including temperature, time, catalyst loading and stirring speed were investigated in order to improve productivity of hydrocarbons within boiling range of diesel fraction. Results of the decarboxylation process showed a very high yield of ~70% of the diesel fraction strongly proving great activity and selectivity of the mesohydrotalcite catalyst. Some other techniques including WAXRD, TEM, BET, CO_2-TPD and NH_3-TPD were also applied to characterize some important properties of the mesohydrotalcite catalyst. They were all evidences for convincing the catalyst ability in the production of biofuel from renewable sources.

Graphical Abstract



Adsorption-desorption isotherm and pore distribution against pore area of MHT-HT catalyst

Highlights

- Preparing mesoporous hydrotalcite based catalyst containing both homogeneous pore channels.
- Narrowing the catalyst pore width from 130Å to 38Å by changing preparation method from

co-condensation evaporation to hydrothermal treatment.
- Establishing decarboxylation of jatropha oil in batch process obtaining green hydrocarbons.
- Yielding 70% of high purity green hydrocarbons in diesel fraction.

Keywords: Mesoporous hydrotalcite, Decarboxylation, Jatropha oil, Hydrothermal, Pore control.

INTRODUCTION

Hydrotalcite based catalysts possessed both acid and base sites which highly suitable with decarboxylation of fatty acids [**1-3, 17, 18**]. However, distribution of these sites on the catalysts surface was restrictive because of their non-existence of ordered porous structure. This reason leaded poor interaction between the active sites and reactants yielding relatively low conversion and selection of the fatty acids to green hydrocarbons. This reason also was drawback with purification of after-reaction products.

Mesoporous materials contributed many advantages which could cope with the disadvantages of the hydrotalcite based catalysts. Once hydrotalcite based catalysts were modified to become ordered mesoporous hydrotalcite like compounds, the catalysts would contain not only acid and base sites, but also ordered mesoporous structure. This structure could highly enhance activity and selectivity of these kinds of catalysts in the decarboxylation of vegetable oil containing fatty acids, leading to produce a high-quality product of rich hydrocarbon composition [**4-6**]. Our paper published elsewhere [**7**] also proved this ability of preparation of the catalysts which could be assigned as mesohydrotalcite catalysts.

Two of the most important characteristics of the mesohydrotalcite catalysts were their acidity and basicity, and pore width distribution [**1, 2, 4**]. Once getting these good properties including suitable acidity and high basicity, and relative medium-sized mesopores, the activity and selectivity of these catalysts in the decarboxylation could be greatly improved. As published in recently paper [**7**], the mesohydrotalcite was successfully synthesized through co-condensation-evaporation method exhibiting its pore width of 138Å. Due to this large pore width compared to kinetic diameter of common triglycerides and fatty acids, there has been essential to improve the pore width of this material [**5**], namely to decrease it into a smaller value.

This paper therefore focused on demonstration of performance of the mesohydrotalcite catalyst before and after its tenability of pore width through testing its ability in conversion of jatropha oil in the decarboxylation process. Once obtaining comparison, the chosen catalyst could be further applied in the investigations of the decarboxylation.

MATERIALS AND METHODS

Preparation of Mg-Al-Comesohydrotalcite catalyst by co-condensation-evaporation method: The mesohydrotalcite catalyst was prepared from basic precursors such as $Mg(NO_3)_2.6H_2O$, $Al_2(SO4)_3.18H_2O$ and $CoCl_2.6H_2O$. Step-by-step procedure for the preparation was briefly described as followed: $Mg(NO_3)_2.6H_2O$, $Al_2(SO4)_3.18H_2O$ and $CoCl_2.6H_2O$ were dissolved in 200 mL of distilled water when Mg/Al/Co molar ratio was fixed at 2/1.8/0.2. The produced solution was then mixed with another solution of 100 mL of distilled water containing 3 g of CTAB. The mixture was transferred to a container supported with temperature-controlled heating mantle, magnetic stirrer. The temperature and stirring speed were set up at 70°C and 600 rpm, respectively. The solution was gradually added with 150 mL solution of NaOH 0.1M until the final pH of the sol reached 9.5± 0.5. After all parameters were stable, timing of 48 h was set up for the reaction. The container was kept in condition of unfluxed evaporation. The finished co-condensation-evaporation would be followed by filtration of liquid from the precipitate. The solid was then dried at 100^{o}C for 24 h. The after-drying solid was then calcined at 500°C for 3 h under heating speed of 2°C min^{-1}. Final powder was then considered as the mesohydrotalcite catalyst prepared by the co-condensation-evaporation method (MHT-CE catalyst).

Preparation of Mg-Al-Co mesohydrotalcite catalyst by hydrothermal treatment: The hydrothermal treatment was applied when keeping some previous parameters and procedure of the co-condensation-evaporation method such as Mg/Al/Co molar ratio of 2/1.8/0.2 and pH of 9.5± 0.5 for the final sol. The mixture was transferred to auto pressurized autoclave and kept at 90°C for 24 h. The precipitate obtained after the hydrothermal treatment was carried out with the same procedures applied to the co-condensation-evaporation method. The catalyst prepared by this method was assigned as MHT-HT catalyst.

Activity tests of MHT-CE and MHT-HT catalysts: The two testing procedures were implemented in the same parameters described as followed: 100 mL jatropha oil was mixed well with 5 grams of the catalyst; the mixture was transferred to an auto pressurized autoclave equipped with heating mantle, thermo couple and stirrer. The decarboxylation was carried out at 400°C for 2 h under stirring speed of 600 rpm. After finishing the reaction, the mixture was cooled to room temperature followed by decantation of liquid phase from solid phase. The liquid product was fractioned by ASTM D 86 to separate fraction having boiling point of 200°C-360°C corresponding to commercial diesel fuel. Yield of the reaction was rawly calculated by comparing this fraction.

Investigations of decarboxylation process: Once reaching the chosen catalyst, it would be applied to investigate the decarboxylation process using jatropha oil. The step-by-step procedures of reaction and purification was familiar with one used in the activity testing process. Differences came from parameters and conditions for the decarboxylation process , Jatropha oil for each investigation: 100 mL; Temperature: from 300°C to 500°C; Timing: 1 h to 3 h; - Load catalyst: 1%wt to 3%wt; Stirring speed: 200 rpm to 800 rpm

Characterizations: Powder XRD were recorded on D8 Advance Bruker diffractometer using Cu Kα (λ = 0.15406) radiation. BET was carried out on Chem BET–3000. GC-MS was established on an Agilent HP 6890 GC-5898 MS supported capillary HT-5MS. Feedstock and product specifications were based on many standards such as ASTM D 1298, D 445, D 97, D 464, D 664, D 93, D 95, D 189, D 2015, E 2583, EN 1411 and EN 12622.

RESULTS AND DISCUSSION

Characterizations of MHT-CE and MHT-HT catalysts: SAXRD patterns were used to prove ordered mesoporous structure of both catalysts. Figure 1 showed their SAXRD patterns.

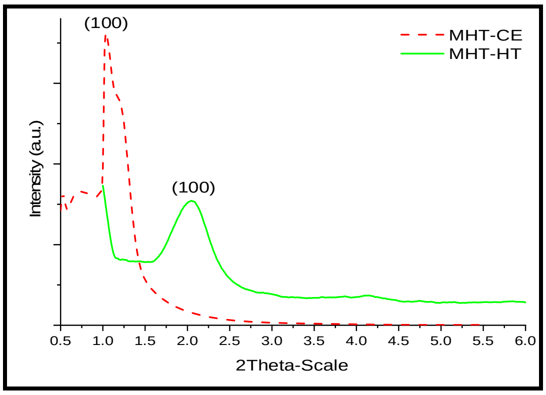


Figure 1. SAXRD patterns of MHT-HT and MHT-CE catalysts

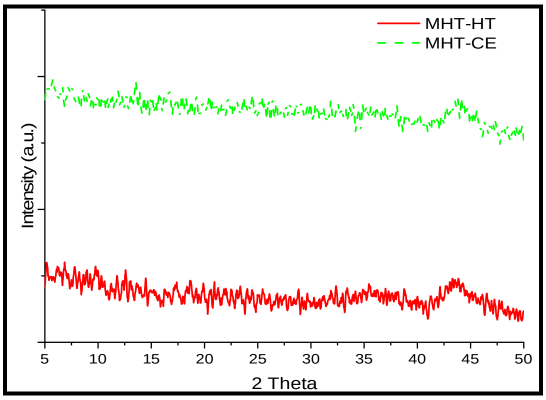


Figure 2. WAXRD patterns of MHT-HT and MHT-CE catalysts.

Both patterns exhibited the ordered mesoporous structure including sharp peaks of (100) reflection planes at 2θ = 1° and 2θ = 2°corresponding to MHT-CE and MHT-HT catalysts, respectively. Difference between these two peaks were increase in the (100) diffraction peak of the MHT-HT catalyst compared to that of the MHT-CE catalyst. The result strongly emphasized that concentrated pore width of the MHT-HT catalyst was narrower than that of the MHT-CE catalyst [8-10], that meaned a successful effort in the modification of the mesoporous hydrotalcite structure. The new pore width distribution would be analyzed for pointing out that it was more adaptable with fatty acid chain in the jatropha oil in the decarboxylation process. However, intensity of the (100) peak of the MHT-HT catalyst was lower than that of the MHT-CE catalyst. The reason was that (and also for the difference between the forms of the two patterns) the hydrothermal treatment was established at high temperature (90°C) compared to that of the co-condensation-evaporation method (70°C).
Figure 2 exhibited WAXRD of both catalysts and showed amorphous structure existence in both of them. These were common structure that would be better for the mesoporous formation.

Porosity analysis of the both catalysts would go along with the XRD patterns for indicating the adaptability between their differences in the SAXRD patterns and the pore width distributions. Figure 3 and 4 described them in forms of surface area pore distribution curves alonging with their adsorption-desorption isotherms.

The MHT-CE catalyst possessed specific surface area of over 270 m^{2}g-1 being relatively low compared to many typical mesoporous materials [10, 16, 19, 20]. However, the reason came from that its structure was constructed by hydrotalcite like compounds, not normal silica's. The pore width concentrated around ~130Å being relatively large compared to the other typical mesomaterials [11-13]. Maximum kinetic diameter of triglyceride could reach ~70Å [8], so the concentrated pore width seemed to be not suitable in the decarboxylation process.

The idea was that a modification of the MHT-CE to MHT-HT catalyst based on that mentioned disadvantages. The MHT-HT catalyst with its concentrated pore width could greatly improve the contact and interaction between reactants and the catalysis active sites.

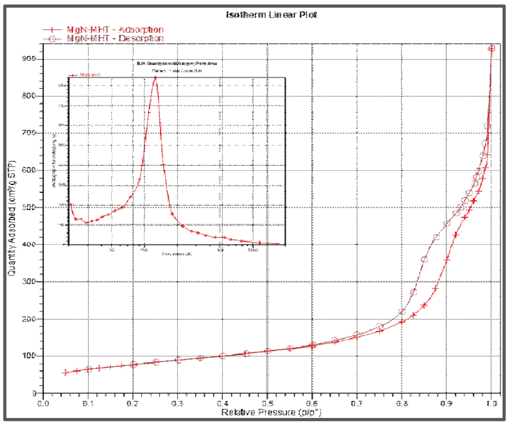


Figure 3. Adsorption-desorption isotherm and pore distribution of MHT-CE catalyst

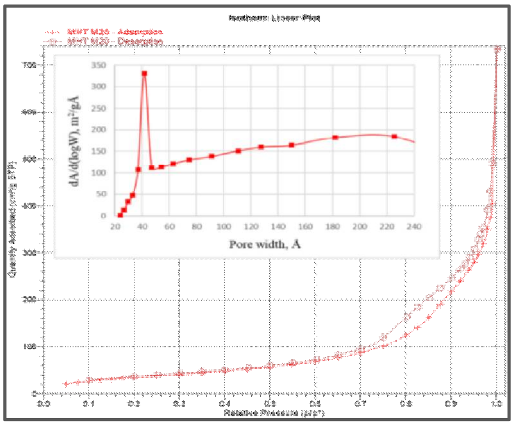


Figure 4. Adsorption-desorption isotherm and pore distribution against pore area of MHT-HT catalyst.

Confidently, concentrated pore width of the catalyst was greatly decreased from the co-condensation-evaporation method to the hydrothermal treatment. In the case of the MHT-HT catalyst, pore width focused around ~38Å. There were some other large pore widths which were suitable with some extra-large triglycerides and fatty acids in the decarboxylation process. Hence, though SAXRD, WAXRD and pore distribution (BET, BJH) techniques, the modification of the MHT-CE to MHT-HT catalyst was clearly demonstrated.

Results from activity test of catalysts: Results obtained from the reaction testing of these two catalysts then could provide the better option for the jatropha oil. These results were collected in table 1.

Table 1. Activity testing results over MHT-CE and MHT-HT catalysts

Product boiling ranges	MHT-CE catalyst	MHT-HT catalyst
<200^{o}C	12.7	8.2
200-360^{o}C	56.9	68.5
>360^{o}C	30.4	23.3

Conditions: 400^{o}C, 2 h, 5g catalyst, 600 rpm

Yield of the main product on 200-360^{o}C fraction sharply increased from the MHT-CE use to the MHT-HT application. That was to say that the better pore distribution could bring a great enhancement to performance of the decarboxylation process. There was no testing for gas composition because there was no gas detector, but the light products in <200^{o}C fraction considerably decreased in the same direction. Besides, using the MHT-HT catalyst could lower the formation of waste products considered as >360^{o}C fraction. These results were caused by the effective modification of the MHT catalyst. The concentrated pore width played an important role in this case; then the MHT-HT had more suitable pores that the MHT-CE had. The hydrothermal process could be better choice for the mesohydrotalcite catalyst.

Results from investigation of the jatropha decarboxylation over MHT-HT catalyst: Jatropha oil was considered as a second-generation feedstock acceptedly applied for biofuel production [14]. Even some publishes declared that jatropha source had no disadvantage in the biofuel sector. Though well recognized feedstock, applications of jatropha oil in the mean of conversion processes were still restrictive. Part of the reason was its superior properties for biodiesel synthesis through transesterification processes. Some properties of the Vietnamese jatropha oil were exploded (Table 2).

Table 2. Properties of the jatropha oil

No.	Specifications	Methods	Values
1	Density	D 1298	0.9079
2	Pour point, ^{o}C	D 97	-11.2
3	Kinetic viscosity at 40^{o}C, cSt	D 445	54.9
4	Acid value, mg/g	D 664	5.5
5	Saponification value, mg/g	D 464	190.1
6	Iodine value, g/100 g	D 5768	122.5
7	Water content, mg/kg	D 95	106
8	Color	Observation	Transparent

The specifications of the jatropha oil were the same as many kinds of common vegetable oil [8], so there was no problem when using it as feedstock in the decarboxylation process. Chemical compositions of the oil were determined by GC-MS method. Table 3 described its collected fatty acid components.

Table 3. Fatty acid composition of jatropha oil

No.	Fatty acids	Contents, %	No.	Fatty acids	Contents, %
1	Undecanoic	0.05	9	Hexadecanoic	0.43
2	Heptadecatriynoic	0.04	10	9,12-Octadecadienoic	23.74
3	9-Hexadecenoic	0.23	11	Octadecanoic	31.46
4	11-Hexadecenoic	9.38	12	9-Octadecenoic	23.65
5	7,10-Octadecadienoic	0.03	13	9,12,15-Octadecatrienoic	1.59
6	Heptadecanoic	0.10	14	11-Eicosenoic	0.21
7	9,11-Octadecadienoic	8.45	15	Eicosanoic	0.45
8	8,11-Octadecadienoic	0.19			

Results in the investigations were briftly collected in table 4 followed by some discussions and explanations about these results.

Table 4. Results on investigations of jatropha oil decarboxylation process

Temperature °C	200-360°C fraction yield, %	Timing h	200-360°C fraction yield, %	Catlyst loaded, %	200-360°C fraction yield, %	Stirring speed, rpm	200-360°C fraction yield, %
300	50.0	1.0	53.3	3.0	54.4	200	57.4
350	60.0	1.5	62.5	3.5	60.2	300	62.8
400	64.9	2.0	69.2	4.0	67.3	400	66.4
450	68.5	2.5	69.07	4.5	70.0	600	70.2
500	65.2	3.0	66.9	5.0	70.0	800	70.2

Figures 5, 6, 7 and 8 also describe dvatiations of the investigated parameters against yield of the 200-360°C fraction. These plots exhibited changes of the diesel fraction yield, and through there suitable values were chosen for applying in the decarboxylation process of jatropha oil.

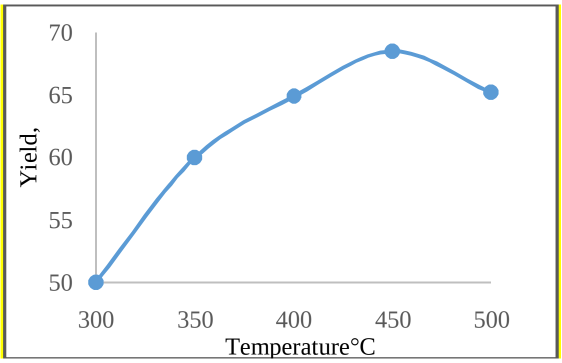


Figure 5. Effect of temperature on diesel fraction yield

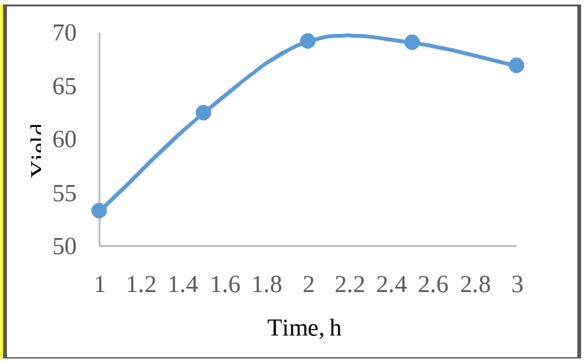


Figure 6. Effect of timing on diesel fraction yield

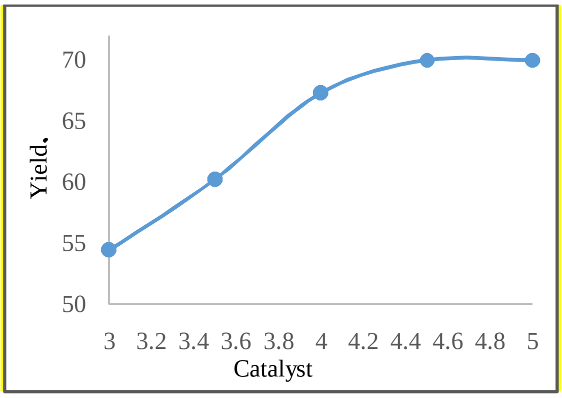


Figure 7. Effect of catalyst dosage on diesel fraction yield

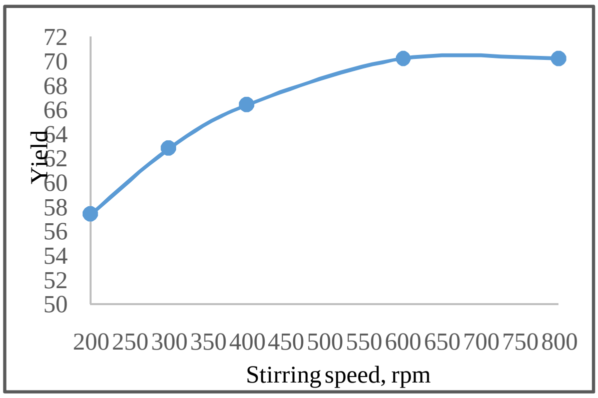


Figure 8. Effect of stirring speed on diesel fraction yield

Examining on the first investigation, the effect of temperature on diesel fraction yield, the yield sharply rose along with the temperature until the temperature reached 450°C, then decreased. General kinetic principle could be applied to explain this phenomenon. Decarboxylation was endothermic processes. Therefore, increasing temperature normally strengthened velocity of the reactions [15, 18]. From 300°C to 450°C, the decarboxylation reactions took advantage over other reactions such as thermal cracking or thermal decomposition. However, when the reaction temperature was over 450°C, these by-reactions could considerably compete with the main decarboxylation process leading to lower the diesel fraction yield.

The diesel fraction yield versus timing was the same behavior to the effect of temperature, with a peak yield arounding 2 h. Explanation could be the same also because some thermal cracking process affected the whole process leading to decrease the diesel fraction yield.Continously, there were gradually increase of the diesel fraction yield when raising the catalyst dosage from 3% to about 4.5%, but this value kept stably when the catalyst content was 5%. The reason was that the catalyst had not only high activity but selectivity, so the kinetic effects were minor even when it reached an excess content.The effect of stirring speed was the same to that of catalyst dosage with the same causes also.

On the whole, the highest yield of fraction of 200-360°C reached ~70% at temperature of 450°C, timing of 2 h, catalyst loaded up to 4.5% and stirring speed of 600 rpm. Comparing to the results obtained from the MHT-CE catalyst published elsewhere, the yield was sharply higher. All obtained or observed results were well fitted with the purposes for the MHT-HT catalyst.

The diesel fraction product was also analyzed by GC-MS method for its chemical components. Table 5 exhibited these compositions, and it really contained many molecules belonging to commercial diesel fuels.

Table 5. Chemical composition of 200-360°C fraction

S. No.	Chemicals	Formulas	Content %wt	S. No.	Chemicals	Formulas	Content %wt
1	1-Tridecene	$C_{13}H_{26}$	2.11	10	Hexadecane	$C_{16}H_{34}$	10.82
3	1-Tetradecene	$C_{14}H_{28}$	6.90	11	Heptadecane	$C_{17}H_{36}$	8.73
2	Tridecane	$C_{13}H_{28}$	7.48	12	Octadecane	$C_{18}H_{38}$	1.4
4	Tetradecane	$C_{14}H_{30}$	3.75	13	Nonadecane	$C_{19}H_{40}$	8.92
5	Pentadecane	$C_{15}H_{32}$	9.89	14	Eicosane	$C_{20}H_{42}$	9.65
6	n-Nonylcyclohexan	$C_{15}H_{30}$	1.59	15	1-Eicosene	$C_{20}H_{40}$	0.65
7	Hexadecene	$C_{16}H_{32}$	15.54	16	10-Heneicosene	$C_{21}H_{42}$	0.49
8	6.9-heptadecadien	$C_{17}H_{32}$	3.80	17	1-Nonadecanol	$C_{10}H_{22}O$	0.37
9	Heptadecen	$C_{17}H_{34}$	7.91				

The GC-MS result of the diesel fraction exhibited mostly hydrocarbons ranging from C_{13} to C_{21} which well fit with the fatty acid composition of the jatropha oil. Therefore, the decarboxylation was successfully established at the chosen parameters. A minor oxygenate component represented a trace incomplete deoxygenation reflecting that the mesohydrotalcite catalyst possessed excellent activity and selectivity in the decarboxylation. Therefore, this fraction could be effectively used for blending with commercial diesel fuel or even for being neat fuel after meeting every diesel fuel specification.

APPLICATION

The synthesized quinoline based 1,2,4-triazole derivatives are useful against the bacterial infections. Research on this type of heterocyclic molecules will be continued.

CONCLUSION

In conclusion, we have efficiently synthesized a series of novel qunoline derivatized 1,2,4-Triazole derivativesin good yield and their antimicrobial activity were evaluated. Synthesized compounds take part in an altered pattern of biological activity compared to the standard drug employed ciprofloxacin. Triazoles **8c**, **8d** and **8h** demonstrated potent inhibition against tested bacteria strains. Only compound **8c** showed good antifungal activity. It can be concluded that incorporation of a 1,2,4-triazole ring into quinoline moiety results in few promising antibacterial molecules. Docking score and binding of the most active compounds into the Gyrase crystal structure of *S. aureus* and *E.coli* is in compatible with the invitro study carried out.

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REFERENCES

[1]. Z. A. Kaplancikli, G. Turan-Zitouni, Ozdemir A, G. Revail, New triazole and triazolo thiadiazine derivatives as possible antimicrobial agents, *Eur. J. Med. Chem.*, **2008**, 43, 155-9.

[2]. R. Mishra, R. Kumar, S. Kumar, J. Majeed, M. Rashid, S. Sharma, Synthesis and In vitro antimicrobialactivity of Some Triazole Derivatives, *J. Chil. Chem. Soc.*, **2010**, 55, 359-362.

[3]. Z. Muhi-Eldeen, M. Nadir, N. R. Aljobory, F. Husseen, S. Stohs, Synthesis of New biologically active Triazoles derivative, *Eur. J. Med. Chem.*,**1991**, 26, 237-241.

[4]. N. Upmanyu, S. Kumar, M. D. Kharya, K. Shah, P. Mishra, Synthesis and anti-microbial evaluation of some novel 1,2,4-triazole derivatives, *Acta. Pol. Pharm.*, **2011**, 68, 213-21.

[5]. M. Abdul Rahiman, D. R. Mamatha, G. L. Thejashree, M. G.Suresha, Synthesis, Characterization and Antimicrobial Studies of Some Novel Thiadiazoles derived from [1,2,4] Triazoles, *J. Applicable Chem.*,**2017**, 6, 01-07.

[6]. L. Zahajska, V. Klimesova, J. Koci, K. Waisser, J .Kaustova, Synthesis and antimycobacterial activity of pyridylmethylsulfanyl and naphthylmethylsulfanyl derivatives of benzazoles, 1, 2, 4-triazole, and pyridine-2-carbothioamide/-2-carbonitrile, *Arch. Pharm.(Weinheim)*, **2004**, 337, 549-55.

[7]. A. Foroumadi, Z. Kiani, F. Soltani, Antituberculosis agents VIII. Synthesis and in vitro antimycobacterial activity of alkyl alpha-[5-(5-nitro-2-thienyl)-1,3,4-thiadiazole-2-ylthio] acetates, *Il Farmaco*, **2003**, 58, 1073-6.

[8]. S. D. Joshi, H. M. Vagdevi, V. P. Vaidya, G. S. Gadaginamath, Synthesis of new 4-pyrrol-1-yl benzoic acid hydrazide analogs and some derived oxadiazole, triazole and pyrrole ring systems: a novel class of potential antibacterial and antitubercular agents, *Eur. J. Med. Chem.*,2008, 43, 1989-96.

[9]. B. P. Mallikarjuna, B. S. Sastry, G. V. Suresh Kumar, Y. Rajendraprasad, S. M. Chandrashekar, K. Sathisha, Synthesis of new 4-isopropylthiazole hydrazide analogs and some derived clubbed triazole, oxadiazole ring systems--a novel class of potential antibacterial, antifungal and antitubercular agents, *Eur. J. Med. Chem.*,**2009**,44, 4739-46.

[10]. G. V. Suresh Kumar, Y. Rajendraprasad, B. P. Mallikarjuna, S. M. Chandrashekar, C. Kistayya, Synthesis of some novel 2-substituted-5-[isopropylthiazole] clubbed 1,2,4-triazole and 1,3,4-oxadiazoles as potential antimicrobial and antitubercular agents, *Eur. J. Med. Chem.*, **2010**,45, 2063-74.

[11]. E. Pomarnacka, M. Gdaniec, Synthesis and anticancer activity of 2-amino-8-chloro-5,5-dioxo[1,2,4]triazolo[2,3-b][1,4,2]benzodithiazine derivatives, *Bioorg. Med. Chem.*, **2003**, 11, 1259-67.

[12]. B. S. Holla, K. N. Poojary, B. Sooryanarayana Rao, M. K. Shivananda, New bis-amino mercaptotriazoles and bis-triazolothiadiazoles as possible anticancer agents, *Eur. J. Med.Chem.*, **2002**, 37, 511-7.

[13]. B. S. Holla, B. Veerendra, M. K.Shivananda, B. Poojary, Synthesis characterization and anticancer activity studies on some Mannich bases derived from 1,2,4-triazoles, *Eur. J. Med.Chem.*,**2003**, 38, 759-67.

[14]. M. F. El-Shehry, A. A.Abu-Hashem,E, M,El-Telbani, Synthesis of 3-((2,4-dichlorophenoxy) methyl)-1,2,4-triazolo(thiadiazoles and thiadiazines) as anti-inflammatory and molluscicidal agents, *Eur. J. Med. Chem.*, **2010,**45, 1906-11.

[15]. J. Chen, X. Y .Sun, K. Y. Chai, J. S. Lee, M. S. Song, Z. S.Quan, Synthesis and anticonvulsant evaluation of 4-(4-alkoxylphenyl)-3-ethyl-4H-1,2,4-triazoles as open-chain analogues of 7-alkoxyl-4,5-dihydro[1,2,4]triazolo[4,3-a]quinolines,*Bioorg. Med .Chem.*, **2007**, 15, 6775-81.

[16]. G. L. Almajan, S. F. Barbucenau, E. R.Almajan, C. Draghici, G. Saramet, Synthesis, characterization and antibacterial activity of some triazole Mannich bases carrying diphenylsulfone moieties, *Eur. J. Med. Chem.*, **2009**, 44, 3083-3089.

[17]. M. Kritsanida, A. Mouroutsou, P. Marakos, N. Pouli, S. Papakonstantinou-Garoufalias, C. Pannecouque, M. Witvrouw, E. De Clercq, *Il Farmaco,* **2002**,57, 253-257.

[18]. B. M.Rao, S.Sangaraju, M.K.Srinivasu, P.Madhavan, M. L.Devi, P. R.Kumar, K. B.Candrasekhar, C.Arpitha,T. S.Balaji, Development and validation of a specific stability indicating high performance liquid chromatographic method for rizatriptan benzoate,*J. Pharm.Biomed.Anal.,***2006**, 41, 1146.

[19]. G. Hancu, A. Gaspar, A. Gyeresi, Separation of 1,4-benzodiazepines by micellarelektrokinetic capillary chromatography, *J.Biochem.Biophys.Methods*, **2007**, 69, 251-9.

[20]. Z. Z.Wang, Y. P.Wang, B.Yang, J. P.Wan,J.Wang, Clinical efficacies of treating refractory insomnia patients with estazolam plus alternating current magnetic field, *Chinese Med. J.*, **2012**,125, 3175-6.

[21]. E. Bajetti, N. Zilembo, E. Bichisao, P. Pozzi, L. Toffolatti, *Critical Reviews in Oncology Hematolog,* **2000**, 33, 137-168.

[22]. Ó. García-Algar, M. Á.López-Vílchez, I.Martín, A.Mur, M.Pellegrini, R.Pacifici, S. Rossi, S .Pichini, *Clinical Toxicol,* **2007**, 45, 295-8.

[23]. A. Demirbas, S. Ceylan , N. Demirbas,,Synthesis of some new five membered heterocycles, a facile synthesis of oxazolidinones, *J.Heterocycl. Chem*, **2007**, 44, 1271-1280.

[24]. C. Foulon, C. Danel, C. Vaccher, S. Yous, J. P.Bonte,J, F, Goossens, Determination of ionization constants of N-imidazole derivatives, aromatase inhibitors, using capillary electrophoresis and influence of substituents on pKa shifts, *J, Chromatograph A.*, **2004**,1035, 131-136.

[25]. L. T. Yu, M. T. Ho, C. Y. Chang, T. K. Yang, Asymmetric zinc Reformatsky reaction of evanschiral imide with acetophenones and its application to the stereoselective synthesis of triazole antifungal agents, *Tetrahedron: Asymmetry,* **2007**, 18, 949-962.

[26]. A. Gupta, J. D. Unadkat, Q. Mao, Interactions of azole antifungal agents with the human breast cancer resistance protein (BCRP),*J. Pharm.Sci,***2007**, 96, 3226-35.

[27]. S. D. Schiller, H. B. Fung, Antimicrobial and antiurease activities of newly synthesized morpholine derivatives containing an azole nucleus, *Clinical Therapeutics,* **2008**, 29, 1862-1886.

[28]. H. A. Torres, R. Y. Hachem, R. F .Chemaly, D. P. Kontoyiannis, Posaconazole: a broad-spectrum triazole antifungal, *Lancet Infect Dis*, **2005**, 5, 775-85.

[29]. D. T. Hsieh,E. A. Thiele, Efficacy and safety of rufinamide in pediatric epilepsy, *Ther Adv Neuro Disord.*, **2013**,6, 189-98.

[30]. S. S. Joshi, A. V. Karnik, Rapid and efficient microwave-assisted synthesis of 4-amino-3-mercapto5-substituted-1,2,4-triazoles, *Indian J. Chem.*, **2006**, 45B, 1057-1059.

[31]. A. Kshirsagar, M. P. Toraskar, V. M. Kulkarni, S. Dhanashire,V. Kadam, *Int. J. Chem. Tech.Res.*, **2009**,1, 696-701.

[32]. A. K. Shirsagar, M. P. Toraskar, *Int. J.Chem.Tech. Res*, **2009**, 1, 696-701.

[33]. S. Ebrahimi, Synthesis of some pyridyl and cyclohexyl substituted 1,2,4 triazole, 1,3,4-thiadiazole and 1,3,4-oxadiazole derivatives, *Eur. J. Chem.,***2010**, 1, 322-324.

[34]. I. Mir, M. T. Siddiqui, Antituberculosis agents. I. Alpha-(5-(2-Furyl)-1,2,4-triazol-3-ylthio) acethydrazide and related compounds, *Tetrahedron,* **1970**, 26, 5235-8.

[35]. K. Ilango, P. Valentina, Synthesis and biological activities of novel 1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazoles, *Der Pharma. Chem.*, **2010**, 2, 16-22.

[36]. M. N. Zemtsova, P. L. Trakhtenberg, M. V. Galkina, A Procedure of 2-methylquinoline-4-carboxylic acids, *Russn. J. Org. Chem.*, **2003**, 49, 1803.

[37]. L. P. Carrod, F. D. Grady. Antibiotics and Chemotherapy, third ed, Churchill Livingstone Edinburg, **1972**, 477.

[38]. N. S. Habib, R. Soliman, A. E. Tombary, S. A. E. Hawash, G. Omaima, O. G. Shaaban, *Arch Pharm Res.*, **2007**, 30, 1511-1520.

[39]. G. Shivaraja, S. Sreenivasa, A. R. Ramesha, T. M. Chakrapani Rao, H. Nagabhushana, Regioselective Synthesis, Antibacterial, Molecular Docking and Fingerprint Applications of 1-Benzhydrylpiperazine Derivatized 1,4-Disubstituted 1,2,3-Triazoles, *Chemistry Select.*, **2018**, 3, 8111 – 8117.

[40]. H. C. Anitha, S.Sreenivasa, N. R. Mohan, Vivek Chandramohan, G. Shivaraja,Preliminary Evaluation of Antimicrobial, Anthelmintic, Anti-Inflammatory Activities and In Silico Studies of Some Cinchoninic Acid Derivatives, *J. Applicable Chem.*, **2017**, 6, 543-558.

[41]. S. Sreenivasa, G. Shivaraja, V. Chandramohan, S. N. Shwetha, Aliyaarif, K. S. Guruprasad, *J. Applicable Chem.*, **2016**, 5, 1089-1096.

[42]. S. D. Sawant, A. A. Barvrkar, A. R. Chabukswar, S. D. Sarak, *J. Applicable Chem.*, **2013**, 2, 372- 384.

[43]. B. Sushma, Ch.V. Suresh, *J. Applicable Chem.*, **2012**, 1, 167-173.