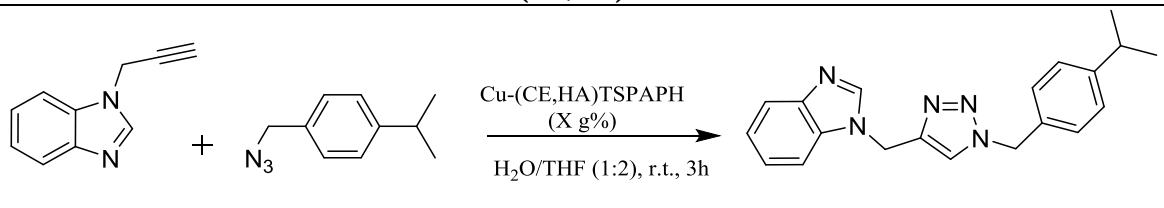
Synthesis of waste shrimp-derived hard filler cross-linker hydroxyapatite for incorporation with cellulose tethered to cuprous silica propyl amino ethoxy ethyl amine as a novel hybrid nano-catalyst for highly efficient synthesis of new 1,2,3-triazolyl N-alkyl benzimidazole hybrid analogues as antifungal

Abstract: The preparation characterization and application of shrimp derived hard filler cross-linker hydroxyapatite (HA)for incorporation with cellulose (CE) tethered to cuprous silica propyl 2-aminophenol (Cu-(CE,HA)TSPAPH) as a novel hybrid nano catalyst for synthesis of new 1,2,3-triazolyl N-alkyl benzimidazole hybrid analogues as potential antifungal agents have been described. Cu-(CE,HA)TSPAPH is fully characterized by different microscopic, spectroscopic and physical techniques, including scanning electron microscopy (SEM), transmission, X-ray diffraction (XRD), Energy-dispersive X-ray spectroscopy (EDS), thermogravimetric analysis (TGA) and FT-IR. This catalyst is utilized to produce the new 1,2,3-triazolyl N-alkyl benzimidazole hybrid analogues. The 'Click' huisgen cycloaddition reaction of benzimidazole with some azidoalkyls in a THF-water media at R.T. prepare the products in better to outstanding yields applied Cu-(CE,HA)TSPAPH. Cu-(CE,HA)TSPAPH is proved to be a stable, low cost, reusable and environmentally benign hybrid catalyst.【Method】Shrimp skin waste (SHW) is abundantly available and freshly collected from local Shrimp markets in Karaj/Alborz province in north of Iran. It was completely washed and soaked in hot deionized water to eliminate flesh, salts, gelatinous and other mucky substances. Then the SHW for 48 hours was left to anhydrous air in the laboratory. In the next step, the SHW were floured by a ball mill. Then, the SHW flour was deproteinized through the external washing with 0.1 M HCl and washed multiple times with distilled water. The residual proteins of SHW were treated with 10% (w/v) NaOH, stirred and heated moderately for two days at 75°C filtered and rinsed with distilled water and dried at 75°C. For the next step, the remaining white powder were heated at alkaline conditions (50% (w/v) NaOH). Subsequently the white precipitate was calcined at 110°C and stirred for 4h. The acquired white powder (HA) was washed thoroughly with deionized water until became neutral and then dried at 70°C. In short, after incorporation CE powder with by a ball mill with HA, the mixture was suspended in 200 mL toluene solution, then, were added to solutions. In the next step, 3-(chloropropyl) trimethoxysilane (SP) was incorporate under a dry nitrogen atmosphere. The mixture was refluxed for 48 h and the resulting solid was separated with a sintered glass, and washed with dry toluene to eliminate the unreacted residue of SP reagent. The remained white precipitates were dried *in vaccu* at 135°C. In the next step white precipitates was suspended in 150 mL of the toluene solution, then 2-aminophenol (APH) was added. The mixture was refluxed for 48 h and the resulted solid was separated with a sintered glass, and washed with dry toluene to remove the unreacted residue of APH reagent. The obtained compound was vacuum dried at 120°C. Afterward, the CuI salt was first dissolved in 50 mL acetonitrile solution under refluxed for 48h and then the obtained mixture from the previous step was gradually added to this mixture. Then the resulted solid was separated with a sintered glass, and washed with anhydrous acetonitrile (4×150 mL) to remove the unreacted residue of CuI reagent and then The obtained Cu-(CE,HA)TSPAPH were vacuum dried at 100°C. 【Result】Shrimp skin waste is abundantly available and freshly collected from local Shrimp markets in Karaj/Alborz province in north of Iran. It was highly washed and soaked in hot deionized water to clean of flesh, salts, gelatinous and dirty substances. The Shrimp skin waste were left to dry air in the laboratory for 48 h and then were powdered by a ball mill. Afterward, the Shrimp skin waste powder (SHWP) was deproteinized through the external washing with HCl and rinsed several times with distilled water. The remaining proteins of SHWP were treated with NaOH stirred and heated moderately for two days at 100 °C, filtered and washed with distilled water and dried at 75 °C. In the next step, the acquired

white SHWP was washed thoroughly with deionized water until became neutral and then dried at 75 °C. Microcrystalline cellulose (CE) were incorporated by a ball mill with HA and then suspended in 150 mL toluene solution, then, 3-(chloropropyl) trimethoxysilane (SP) was added under a dry nitrogen atmosphere. The mixture was refluxed for 48 h and the resulting solid was incorporated with 2-aminophenol (APH). The mixture was refluxed for 48 h and the resulted solid was separated with a sintered glass, and washed with dry toluene to remove the unreacted residue of APH reagent. The obtained compound was vacuum dried at 120°C. Afterward, the CuI salt was first dissolved in 50 mL acetonitrile solution under refluxed for 48h and then the obtained mixture from the previous step was gradually added to this mixture.【Conclusion】In conclusion, the general mechanism explaining the application of Shrimp skin waste to obtain the hydroxyapatite for synthesis, characterization and application of for incorporation with cellulose tethered to cuprous silica propyl 2-aminophenol (Cu-(CE,HA)TSPAPH) as a novel hybrid nano catalyst. This catalyst has been used in synthesis of new 1,2,3-triazolyl N-alkyl benzimidazole hybrid analogues.

Key words: shrimp, hydroxyapatite, cellulose, 1,2,3-triazolyl N-alkyl benzimidazole hybrid analogue, Cu-(CE,HA)TSPAPH, Azidoalkyl

Tab. 1 Influence of catalyst amount in synthesis of 1,2,3-triazolyl N-alkyl benzimidazole hybrid using Cu-(CE,HA)TSPAPH



Entry	Cu-(CE,HA)TSPAPH (g)	Time(h)	Yield(%)[d]
1	0.02	4	75
2	0.03	4	75
3	0.04	4	85
4	0.05	4	90
5	0.06	4	95
6	0.07	4	95
7	0.08	4	95

[a] Reagents and conditions: 1-(Prop-2-yn-1-yl)-1H-benzo[d]imidazole , (0.01 mol), 1-(azidomethyl)-4-isopropylbenzene (0.011 mol), Cu-(CE,HA)TSPAPH (x g), THF/H2O (2:1, 30 mL), room temperature, 4 h, [b] Isolated Yield

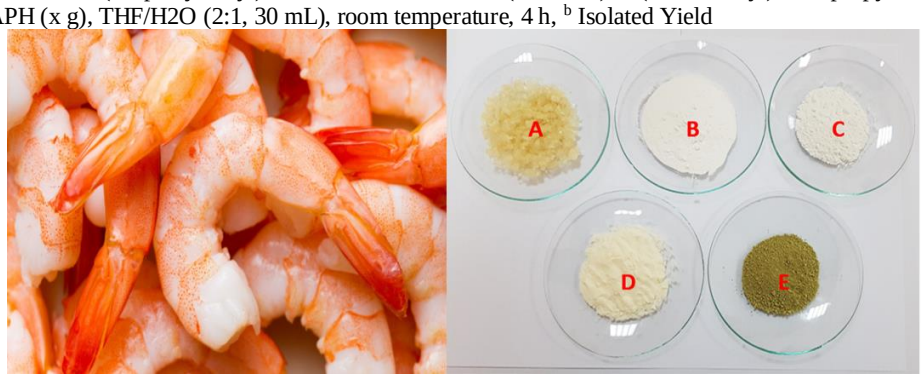


Fig. A Color changes from Shrimp skin waste (**A**) to Cu-(CE,HA)TSPAPH (E)

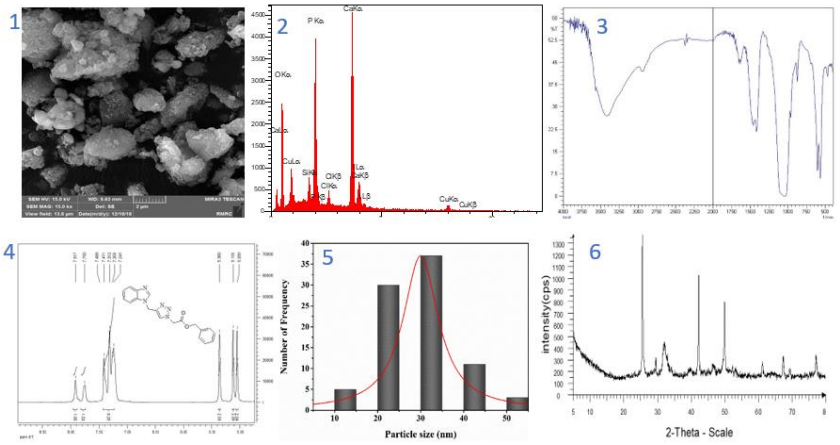


Fig. B Scanning electron microscopy (SEM) image (1), EDS spectrum (2), FT-IR spectrum (3), ^{1}H-NMR spectrum of one of the compound (4), Histogram representing the average diameter (5) and XRD Pattern of the Cu-(CE,HA)TSPAPH

The scanning electron microscopy (SEM) was applied to show the morphology and size of the Cu-(CE,HA)TSPAPH (Fig. B-1). As shown, the particle sizes of the catalyst powders are at a nanoscale and they are non-spherical in morphology. Based on the histogram (Fig. B-5) obtained from the SEM analysis and also using the microstructural image processing software (MIP software), the particle size distribution was found to be around 15-45 nm. The chemical composition of nanoparticles was also determined using energy-dispersive X-ray (EDS). The EDS analysis revealed the presence of C, Si, N, O, S, Ca, P and Cu elements which is a good evidence for the synthesis of Cu-(CE,HA)TSPAPH spectroscopy. The powder XRD pattern of Cu-(CE,HA)TSPAPH is shown in Fig. B-6. The reflections due to the HA phase were observed at the courier peaks of 2Θ values of 25.43°, 29.44°, 32.83°, 42.159°, 49.89°, 52.24°, 67.34°, 69.36° and 77.12° corresponding to the crystal planes of (865), (95), (43), (651), (481), (37), (131), (36) and (142), respectively. It is also worthy to mention that it is hard to distinguish the tethered Cu to organic phases (CE) in catalyst due to peaks overlap between copper species and HA.

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