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Investigation of antimicrobial activity of Nano sized particles of oxindoles and compression their activity with tetracycline and gentamic in drugs

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ABSTRACT: We reported clean one-pot technique for the preparation of nano particles of oxindole derivatives by using isatins and indoles in the presence of constant current as catalyzer. The product was characterized after purification using IR, 1H NMR, 13C NMR, MS, and SEM. the synthesized compounds have been screened for their antibacterial activities Some of nano particles of oxindole were showed antimicrobial activities against some gram positive and negative bacteria's.

Keywords: Oxindoles, Constant Current, Antimicrobial, Nanoparticles

INTRODUCTION

In the family of heterocyclic compounds nitrogen containing heterocyclic are an necessary class of compounds in the medicinal chemistry and also contributed to the people from biological and industrial point which helps to understand life processes (Heda *et al.,* 2009). Indole is an vital heterocyclic system because it is built into proteins in the type of amino acid tryptophan, because it is the basis of drugs like indomethacin and because it provides the skeleton of indole alkaloids biologically active compounds from plants including strychnine and LSD (Sharma *et al.,* 2010). The incorporation of indole nucleus, has completed it flexible heterocyclic with wide biological activities for example Anti-inflammatory and analgesic (Abele *et al.,* 2003, Amir *et al.,* 1997, Antifungal (Abele *et al.,* 2003, Skii *et al.,* 1997), Antimicrobial (Panwar *et al.,* 2006, Hiari *et al.,* 2006), Insecticidal activity (Abele *et al.,* 2003, Sharma *et al.,* 1992), Anticancer (Abele *et al.,* 2003, Hong *et al.,* 2006, Garcia and Martinez 2002, Rossiter *et al.,* 2002, Queiroz *et al.,* 2008), 5-Lipoxygenase inhibitors (Zheng *et al.,* 2007)., Anti HIV (Abele *et al.,* 2003, Merino *et al.,* 1999), Antioxidant (Enein *et al.,* 2004, Talaz *et al.,* 2009), Ant tubercular (Abele *et al.,* 2003, Karali *et al.,* 2007), Antiviral (Abele *et al.,* 2003).

A lot of pharmaceutical companies are performing study to decline the particle size of Nano powders, which are solid particles that measure on the nano scale. Drugs with smaller particle sizes would be better absorbed by the digestive tract lining, thus reducing the amount crucial and making medicines more reasonable (Pison *et al.,* 2006). Decreasing particle size could enhance bioavailability drastically; producing faster-reacting drugs with various applications in the health industry (Azzam *et al.,* 2011).The ability to deliver antibiotics in aerosol form to the lungs would provide an easier way of treating infections like tuberculosis (Reverchon *et al.,* 2002).

This point describes antibacterial activities of oxindoles synthesized by electrochemical methods directly from original compounds to contrast its biological properties with common antibiotic drugs like Tetracycline and Gentamicin.

METHODS

A. Chemicals and materials

Constant current coulometer and preparative electrolysis were performed using a SAMA potentiostate/galvanostate (Isfahan, Iran). The working electrodes were an iron cathode (5 cm^2) and a magnesium anode (5 cm^2). The IR spectra were recorded on a Bruker IFS-66 FT-IR spectrophotometer. NMR spectra were recorded on a Bruker DRX-300 Advance instrument. Mass spectra were obtained using a QP-1100 EX Shimadzu GC-MS (EI at 70 eV) and an hp (Agilent Technologies) 5937 mass selective detector. Scanning electron microscopy (SEM) was run with an axl30 scanning electron microanalyses (Philips, Netherlands) at an acceleration voltage of 20.0 kV.

The melting point of the produce was obtained using an electro thermal melting point apparatus, model 9200. All compounds were commercially available, obtained from Merck and used without additional purification.

RESULTS AND DISCUSSION

A. General procedure for synthesis of nanoparticles of oxindoles

A mixture of indole (1 mmol), 5-bromoisatin (1 mmol), and NaBr (0.5 mmol) in propanol (25 cm^3) was stirred and electrolyzed in an undivided cell equipped with an iron cathode and a magnesium anode at 40°C under a constant current density of 10 mA cm^{-2} (I = 50 mA). After the finishing point of the reaction (monitored by TLC, ethyl acetate/n-hexane 2:1), the solvent was evaporated under reduced pressure, ethanol (90%) was added to the reaction mixture and the ensuing solid was centrifuged. The crude products were then gathered for analysis figure 1(Makarem *et al.*, 2012).

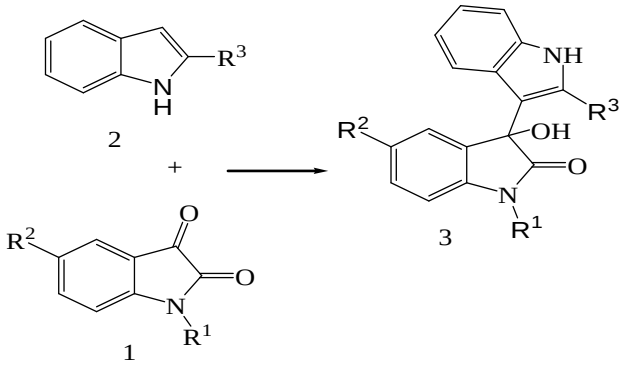

Fig. 1. Synthesis of nano particles of oxindole.

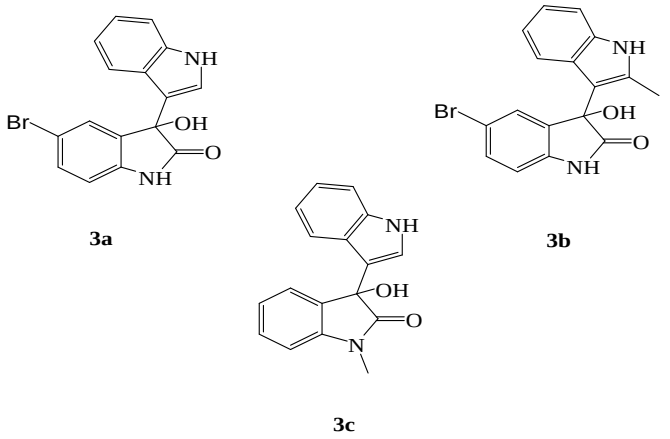

Fig. 2. Structure of 3a-3c.

In continuance of our preceding studies on the development of electro synthesis for synthesis of nanoparticles of organic compounds we screened antimicrobial activities of nanoparticles of 3a-3c figure 2.

B. Antimicrobial studies of nano sized particles of oxindole

In this schoolwork, six microorganisms were used such as *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 85327 (Gram negative bacteria), *Bacillus subtilis* ATCC 465 and Staphylococcus aureus ATCC 25923, *Klebsiella pneumonia* ATCC 29655 and *Enterococcus faecalis* (ATCC 29737) (Gram positive bacteria).oxindoles were dissolved in DMSO (100 µg/ml), and 25 µl was loaded onto 6-mm paper discs. One hundred micro liters of 109 cell/ml suspension of the microorganisms was increase on sterile Mueller-Hinton agar plates, and the discs were placed on the surface of culture plates.

The inhibition zone of compounds in the region of the disc are shown in Table 1 which compared with three profitable antibiotics such as Tetracycline and Gentamicin. Compounds 3a and 3c display activity against *B. subtilis, S. aureus, K. pneumonia, E. coli, P. aeruginosa* and *E. faecalis*.

The minimum inhibitory concentration (MIC) of the selected compounds which showed antibiotic action in disc diffusion tests were also determined by microdillution method (Makarem *et al.*, 2012) to contrast with three marketable antibiotics: Tetracycline and Gentamicin. The results are shown in Table 2.

Table 1: Inhibition zones (mm) of synthesized nano sized particles of oxindole against gram Positive and negative bacteria's by disc diffusion method.

Compound	*Bacillus subtilis* (ATCC 465)	*Staphylococcus aureus* (ATCC 25923)	*Escherichia coli* (ATCC 5922)	*Enterococcus faecalis* (ATCC9737)	*Pseudomonas aeruginosa* (ATCC 85327)	*Klebsiellapne umoniae* (ATCC9655)
3a	15	25	22	20	17	19
3b	0	0	0	0	0	0
3c	12	16	18	14	9	16
Tetracycline	21	20	0	9	0	8
Gentamicin	0	0	23	0	12	0

Table 2: Minimum inhibitory concentrations (µg/mL) of synthesized nano sized particles of oxindole against gram positive and negative bacteria's.

Compound	*Bacillus subtilis* (ATCC 465)	*Staphylococcus aureus* (ATCC 25923)	*Escherichia coli* (ATCC 25922)	*Enterococcus faecalis* (ATCC 29737)	*Pseudomonas aeruginosa* (ATCC 85327)	*Klebsiellapneum oniae* (ATCC 29655)
3a	32	<2	<2	<2	8	2
3b	-	-	-	-	-	-
3c	32	8	2	32	128	4
Tetracycline	4	4	NT[c]	8	NT[c]	16
Gentamicin	NT[c]	NT[c]	4	NT[c]	8	NT[c]

[c] Not Tested

CONCLUSION

at the present time, growing resistance of pathogens against anti-bacterial compounds used is a common and vital problem, which shows obviously that research on new com-pounds against these pathogens is needed. We synthesized 3 substituted Nano sized particles of oxindoles and screened their antimicrobial activities, nanoparticles of 3a-3c display antimicrobial activities against some gram positive and negative bacteria's and compound 3a shows antimicrobial activities better than Tetracycline and Gentamicin.

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