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SYNTHESIS AND CHARACTERIZATION OF NANOPARTICLES OF B-D-LACTOSYL THIOCARBAMATES

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ABSTRACT
Antimicrobial activity address the crucial problem of increasing microbial resistance against antibiotics. The study includes the comparison of synthesized nanoparticles of Lactosyl thiocarbamates & Lactosyl thiocarbamides with its bulk. It appeared interesting to carry out the antimicrobial activity, which shows the improvement in Lactosyl nanoparticles than bulk one. The characterization of new thiocarbamates and biologically made nanoparticles has been carried out by usual chemical transformation, NMR, IR and Mass spectral studies and the characterization of prepared nanoparticles were done by antimicrobial activity, melting point difference, X-ray diffraction and U. V. spectroscopy.

Keywords— Thiocarbamates, thiocarbamides, nanoparticles, lactose

I. INTRODUCTION
In recent years, there has been a considerable interest in the field of Nanotechnology. As defined by size is naturally very broad, including field of science as diverse as surface science, organic chemistry, molecular biology, semiconductor physics, energy storage, micro fabrication, molecular engineering etc. Highly reactive nature of N-linked sugar isothiocyanate and isocyanate appears to promise its great applicability in the synthesis of thiocarbamates and carbamates which find the wide spread use in pharmaceutical industries. Has the potential to make a great impact on human health, ranging from prevention to diagnosis and treatment of disease. Antimicrobial activity tests confirms how effective a drug is. The application of nanotechnology in medicine Isothiocyanates and isocyanates are a group of very reactive chemical compounds. Once they have reacted, the resulting product is usually less harmful than the chemical itself. This chemical is used in the manufacture of carbamates and thiocarbamates. Due to high reactivity towards compounds containing active hydrogen atom isocyanates and isothiocyanates are one of the most versatile classes of functional groups. The high yields and lack of byproducts with this type of reaction have led to their commercial exploitation in the polymer field, agrochemicals and pharmaceuticals. Reactions with carbon nucleophiles provide a useful synthetic access to substituted amides and other derivatives.

Sugar isothiocyanates rank among the most versatile synthetic intermediates in carbohydrates chemistry1-3. They plays a vital role in the preparation of a broad series of functional groups such as thioamides4, isonitrile, carbodiimide and N-thiocarbonyl derivatives5-7 allowing, simultaneously, the covalent coupling of a quite unrestricted variety of structures to the saccharide part. More ever, isothiocyanates are important reagents in heterocyclic chemistry8-9 which may be exploited in the synthesis of nucleosides10 and other N-glycosyl11-12 structures. Dialdehyde starch nanoparticles are useful carrier for anticancer drug because of their small size, good thermal stability, low biological toxicity and slowly anticancer drug releasing to strengthen drug effect13.

II. EXPERIMENTAL
Determining the difference between melting point of compounds and their nanoparticles is one way to test if the nanoparticle is prepared or not. So the M.P. of compounds and their nanoparticles has been taken using melting point apparatus. The prepared Compounds and their nanoparticles have been screened for antimicrobial activity using Cup plate agar diffusion method. By measuring zone of inhibition in mm antimicrobial activity has been studied. By using DMSO as a solvent the concentration of compound were 1 mg/ ml. Amikacin (100 µg/ml) was used as a standard. Compounds were screened for antimicrobial activity against microbes (listed in table 2) in nutrient agar medium. H1 NMR data of the compounds were measured using CDCl3 solvent on 300 MHz frequency. And their chemical shift values are in (ppm) units using TMS as a reference. IR spectral data of the compounds were recorded on FTIR-RXI spectrophotometer. Confirmation of products and reaction progress carried out by TLC using Hexane : Ethyl acetate solvent system and identification of spots carried out by using iodine chamber, UV chamber and KMnO4 spray.

III. METHOD OF PREPERATION
Step 1 : preparation of Lactose Octabenzoate: 55 ml dry Pyridine and 55 ml dry Chloroform were taken in a 1 lit. tight cork glass bottle and cooled in an ice-salt bath. To this solution previously prepared cooled solution of 55 ml Benzoyl Chloride in 55 ml dry Chloroform was added with constant stirring. To this mixture 20 gm. of dry powder of Lactose was added in small instalments with constant stirring by maintaining the temperature

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below 5 oC. After 24 hrs. mixture was washed several times with dil. Aq. Sulphuric acid, followed by aq. Sodium Bicarbonate and lastly with water. By using separating funnel Chloroform layer was separated which contains desired product. Product was triturated several times with petroleum ether until white powder obtained with M.P. 112 o C.

Step 2 : Synthesis of hepta-O-benzoyl-α-D Lactosyl Bromide

The fine powdered of lactose octabenzoate (10gm) was added to the brominating agent (4g Red Phosphorus + 40 ml Glacial Acetic acid + 15 ml molecular Bromine). Then flask was kept for 2 hrs at room temperature. Then 70 ml Chloroform was added to the reaction mixture followed by vigorous shaking. The resultant mixture was poured in an ice cold water to separate Chloroform layer. It was washed several times with aq. Sodium bicarbonate to remove excess of acetic acid followed by aq. Sodium metabisulphite to remove excess of bromine and finally 2-3 times with water. By using separating funnel the solution was removed and addition of petroleum ether results a solid mass (20 gm).

Step 3: Synthesis of hepta-O-benzoyl-β-D-lactosyl isothiocyanate: To a suspension of hepta-O-benzoyl-α-D Lactosyl bromide (15gm) in sodium, 60 ml dried xylene and 5g lead thiocyanate was added. The reaction mixture was refluxed for 3 hrs, gentle shaking. Solution was then cooled and liberated lead bromide was removed by filtration. The xylene filtrate was treated with petroleum ether with stirring, a white solid mass obtained. This solid was expected hepta-O-benzoyl-β-D-lactosyl isothiocyanate. M. P. 116-120 o C.

Step 4: Synthesis of N-lactosylated Thiocarbamates and : Reaction mixture of hepta-O-benzoyl-β-D-lactosyl isothiocyanate with various alcohols has been refluxed for 5 hrs. On cooling and mixing with water most of the alcohols gave a white granular solid was purified by Chloroform-Petroleum ether.

Step 5: Synthesis of N-lactosylated Thiocarbamides: Reaction of hepta-O-benzoyl-β-D-lactosyl isothiocyanate and various aryl amines has been carried out in boiling benzene for 3 hrs. The solvent benzene was distilled off and sticky mass was isolated as residue. Then triturated several times with petroleum ether was converted to granular solid. Crystallized from chloroform-ether.

Step 6 : Preparation of Nanoparticles (Biologically) : Small pieces of potato was boiled in little amount of water in a beaker for about 10 min. Filtered the semi hot solution through filter paper, remaining filtrate obtained called potato extract. 1 gm. of compound was dissolved in 2 ml of DMSO, clear solution was obtained. Then 2-3 drops of potato extract was added to the clear solution, suddenly white precipitate of nanoparticles was obtained.

IV. SCHEME

R1= a) ethyl b) methyl c) n-propyl d) isopropyl e) n-butyl f) t-butyl

R2= a) Phenyl b) o-tolyl c) m-tolyl d) p-tolyl e) o-Cl-phenyl f) m-Cl-phenyl g) p-Cl-phenyl

V. RESULT AND DISCUSSION

(Table 1)

Sr. No.	Alcohols	1-hepta-O-benzoyl-β-D-lactosyl-3-aryl thiocarbamates	Yield %	Melting point of Bulk °C	Melting point of Nanoparticles
1.	Ethyl	O-ethyl thiocarbamate	76	125-130	
2.	Methyl	O-methyl thiocarbamate	74	143	
3.	n-propyl	O-n-propyl thiocarbamate	75	158-160	
4.	Isopropyl	O-isopropyl thiocarbamate	78	132-137	143-145
5.	n-butyl	O-n-butyl thiocarbamate	63	128	159-161
6.	t-butyl	O-t-butyl thiocarbamate	67	145	167-170

(Table 2)

Sr. No.	Aryl amines	1-hepta-O-benzoyl-β-D-lactosyl-3-aryl thiocarbamides	Yield %	Melting point of Bulk °C	Melting point of Nanoparticles °C
1.	Aniline	-3-phenyl thiocarbamide	72	125-130	97-99
2.	o-toluidine	-3-o-tolyl thiocarbamide	76	143	122
3.	m-toluidine	-3-m-tolyl thiocarbamide	88	158-160	131-135

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4.	p-toluidine	-3-p-tolyl thiocarbamide	78	132-137	107-110
5.	o-Cl-Aniline	-3-o-Cl-phenyl thiocarbamide	88	128	102-105
6.	m-Cl-Aniline	-3-m-Cl-phenyl thiocarbamide	84	145	128-131
7.	p-Cl-Aniline	-3-p-Cl-phenyl thiocarbamide	87	148-152	130-133

The characterization of compounds have been confirmed by IR spectroscopy which shows C=S, N-H, C-N, C=O, C-O stretching frequencies at different absorption bands. H1 NMR shows signal due to N-H proton at 8.06 ppm and Lactosyl protons at 5.58 – 3.79 ppm. and benzoyl protons at 6.8 – 3.9 ppm. The Characterization of nanoparticles has been carried out by UV visible spectroscopy. The band gap difference increases as the size of nanoparticles decreases. The decrease in melting point confirms the nanoparticles were prepared.

Antimicrobial activity (Thiocarbamates) (Table 3)

Antimicrobials	Bulk	Nanoparticles
E. coli	11 mm	15 mm
S. aureus	11 mm	14 mm
S. typhi	10 mm	14 mm
P. vulgaris	12 mm	15 mm
Amikacin	10 mm	17 mm
Clandamycine	12 mm	18 mm
DMSO	31 mm	24 mm

Antimicrobial activity (Thiocarbamides) (Table 4)

Antimicrobials	Bulk	Nanoparticles
E. coli	10 mm	14 mm
S. aureus	11 mm	16 mm
S. typhi	11mm	15 mm
P. vulgaris	11 mm	16 mm
Amikacin	10 mm	17 mm
Clandamycine	12 mm	16 mm
DMSO	32 mm	23 mm

*Including the well diameter of 8 mm. **Zone of inhibition in mm (15 or less) resistance, (16-20 mm) moderate and (> 20 mm) sensitive.

The prepared Compounds and their nanoparticles have been screened for antimicrobial activity using Cup plate agar diffusion method. By measuring zone of inhibition in mm antimicrobial activity has been studied. By using DMSO as a solvent the concentration of compound were 1 mg/ ml. Amikacin (100 µg/ml) was used as a standard. Compounds were screened for antimicrobial activity against microbes (listed in table 2) in nutrient agar medium. Zone of inhibition of nanoparticles were more than bulk, which confirms better antimicrobial activity of nanoparticles in comparison to bulk one.

VI. CONCLUSION

Nanoparticles shows better antimicrobial activity than bulk. The study includes the comparison of synthesized nanoparticles of Lactosyl thiocarbamates & Lactosyl thiocarbamides with its bulk. Data observed in the observation table shows that nanoparticles of both thiocarbamates and thiocarbamides have improved antimicrobial activity than the bulk one. Carbohydrate nanoparticles are beneficial for the medicinal purposes like anti-cancer, drug delivery system, recognition of antigens and many other pharmacological applications.

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