A Novel Studies of Synthesis of Nanopartical of Some Maltosyl thiobiurets and Their XRD, SEM and Microbial Studies

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Abstract:

The chemistry of thiourea of carbohydrate is extensively elaborated and well documented. The use of microwave irradiation in organic synthesis has become increasingly popular within the pharmaceutical and academic arenas, because it is a new enabling technology for drug discovery and development. A huge number of research papers have appeared over the last decades on the application of microwave technology in organic synthesis. By taking advantage of this efficient source of energy, These compounds arouse interest as potential biologically active substances and versatile intermediates for preparing various derivatives. They have been found useful in the treatment of hypertension, as appetite suppersant and as a potential anti oxidant cardio protective agent. Chemistry of sugar isocyanate with special reference to their utility as intermediate in the synthesis of nitrogen and sulphur containing open chain and cyclic compound. Several lactosyl thiobiurets deravaives has been prepare by condensation of hepta-O-acetyl-B-D-maltosyl isocyanate with various aryl thiocarbamides by microwave method. The identities of newly synthesis co,mpounds have been established on the basis of usual chemical transformation and IR, NMR, Mass spectral studies.

Keywords: *Hepta-O-acetyl-B-D-maltosyl isocyanate, Aryl thiocarbamides , maltosyl thiobiurtes.*

Introduction:-

In recent years, the electromagnetic energy in the range of microwaves have gained special attention as regards the most various fields of utilization such as the alimentary (domestic ovens), analytical (small ovens devoted to the mineralization), and that one of bio-medical applications[1]. In the field of organic synthetic chemistry, a certain delay has been suffered either in the base research for the clear improvements which can lead to higher yields of cleaner products, minor energy consumption, and environmental compatibility This delay can, however be rapidly reduced by use of electromagnetic energy caused by microwaves. Thus microwave energy can be used and is been used as an activating agent in chemistry for the synthesis of a large variety of compound. Numerous organic reaction assisted by microwave heating have been explained in various article and book[2,3]. These concern the acylation and alkylation reaction, aromatic nucleophilic substitution, condensation, cycloaddition, protection, deprotection reaction, esterification and transesterification, heterocyclisation, rearrangement, organometallic reaction, oxidation and reduction[4].

Microwave-assisted organic synthesis (MAOS) has been known since 1986[5]. This non-conventional synthetic method has shown broad applications as a very efficient way to accelerate the course of many organic reactions, producing high yields, higher selectivity and lower quantities of side products consequently easier work-up and purification of the products. MAOS is considered as a green technology, principally since many organic reactions can be carried out in solvent-free conditions[6].

However, a limited numbers of these reaction regard so for the carbohydrate chemistry, and since carbohydrate play an important role in vast array of biological processes, and particularly there are many advantages for example in carbohydrate based drug such as low toxicity and immunogenicity the interest in their preparation is very high, another example may be taken of sugar isothiocyanate and isocyanate which are among the most versatile synthetic intermediate in carbohydrate chemistry. They play a pivotal role in the preparation of a broad series of functional group such as amide, isonitrile, carbodimide and *N*-thiocarbonyl oxidation dyes[7] for printing the padding animal and vegetable fibers by standard oxidation dyeing method. Many of them have also shown antitumor and tuberculostatic activities[8]. *N*-glucosylated compound may be broadly classified into two ways. The first in which glucosyl group is attached to the nitrogen of non-cyclic compound or the exocyclic nitrogen. For example nucleic ring while the second in which glucosyl group is attached to the nitrogen of noncyclic compound or the exocyclic nitrogen. For example nucleosides represent the first category while glucosyl amines, glucosylureides, glycosylthioureides belong to second category.

In view the application of *N*-maltosylated compounds and nanoparticals in medicinal,indrustrial and in many other ways, it appeared interesting to carry out the synthesis of nanoparticals of 1-Hepta-*O*-acetyl-β-D-maltosylaryl thiobiurets.

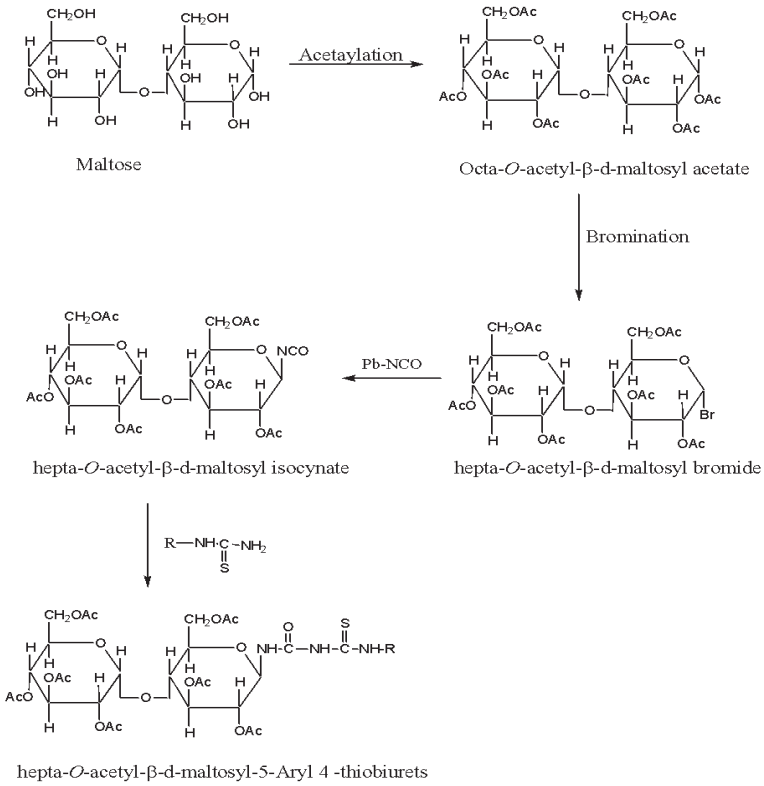
Result and Discussion:-

- **Nanoparticals**

A sub-classification of ultrafine particle with lengths in two or three dimensions greater than 0.001 micrometer (1 nanometer) and smaller than about 0.1 micrometer (100 nanometers) and which may or may not exhibit a size-related intensive property. This term is a subject of controversy regarding the size range and the presence of a size-related property. Current usage emphasizes size and not properties in the definition. The length scale may be a hydrodynamic diameter or a geometric length appropriate to the intended use of the nanoparticle. The European community has discussed the topic and issued a document Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) that offers a more complex approach.

Chemistry of sugar isothiocyanate with special reference to their utility as intermediate in the synthesis of nitrogen and sulphur containing open chain and cyclic compounds has been investigated by earlier workers. It appeared quite interesting to prepare nanoparticals of carbohydrate related compounds, by the extension of already known methods and to investigate the chemistry of these new related compounds with reference to their synthetic application, towards medicinal chemistry.

- **Reaction :-**



R= 1) p-amino Benzoic Acid 2) p-toludine 3) p-Cl-aniline

Several maltosyl thiobiurets deravaives has been prepare by condensation of Hepta-O-acetyl-B-D-maltosyl isocyanate with various aryl thiocarbamides by microwave method. Toluene solution of Hepta-O-acetyl- β -D-maltosyl isocyanate (0.005 M, 1 g) was added to 4amino -1-phenyl thiocarbamide (0.21 gm in 20 ml) and the reaction mixture was under microwave irradiation It was then allowed to cool and pour it in petroleum ether with vigorous stirring; a white granular solid was separated out. The characterization of products was established by IR, ^{1}HNMR, MS XRD Spectral studies.

Experimental

Melting points were recorded on electro thermal melting point apparatus are uncorrected. Specificrotations were measured on Equip-Tronic digital polarimeter model no. EQ 800 at 30^{0}C in $CHCl_3$.

IRspectra were recorded on a Perkin Elmer spectrometer. ^{1}H NMR were obtained on a Bruker DRX-300(300 MHz FT NMR) NMR spectrometer in $CDCl_3$ solution with TMS as an internal reference. The massspectra were recorded on a DART mass spectrometerwere recorded. Purity of the compounds was checkedby thin layer chromatography using Merck silica gel coated aluminum plates and petroleum ether: ethylacetate as eluent.

Synthesis of 1-hepta-O-acetyl-β-D-maltosyl-5-*p*-toludine-4-thiobiuret

Benzene solution of Hepta-O-acetyl- β -D-maltosyl isocyanate (0.005 M, 1.9 g) was added to *p*-toludine (0.25g in 20 ml) and the reaction mixture was under microwave irradiation. It was then allowed to cool and pour it in Petroleum Ether (60-80) with vigorous stirring; a white granular solid was separated out, crystallized from aqueous ethnaol, m.p. 122°C. [Found C, 50.56; H, 5.54; N, 2.39; S, 4.80 $C_{21}H_{26}O_{11}N_3S$; requires; C, 50.30; H, 5.09; N, 2.80; S, 4.40%]

It was found soluble in alcohols acetone, chloroform and benzene while insoluble in water and petroleum ether. It charred when warmed with conc. sulphuric acid. The specific rotation was found to be $[\alpha]_D^{35}$ = - 136° (c, 0.74 in chloroform). The purity was checked by TLC, and recorded Rf value 0.62 (CCl_4: EtOAc 3:2.1)

Analytical And Spectral Data Of Compounds:

- **Synthesis of 1-hepta-O-acetyl-β-D-maltosyl-5-*p*-aminobenzoicacid-4-dithiobiuret**

Yield 72 (%); Mp.135^{0}C;$[\alpha]_D^{32}$252.42°(0.1, in $CHCl_3$);R*f* (Hexane:EtOAC)(1:1)0.59; **IR (KBr)cm- 1**:ν 3000-3292 (Ar-H)str ,1755 (C=O)str, 1543(C=N) str, , 1425 (C-N)str, 927(char. of glucopyranosyl ring), 758 (C=S) str.. **^{1}HNMR (CDCl3)ppm:** 7.46-6.32 (m,8H, Ar-H), 5.57-5.59 (m, 14H, lactosyl-H), 2.31-2.01 (m, 12H,OAc),. **MS**(m/z) : 535 (M+),511, 408, 331, 263, 261, 169, 108.(Anal.Calcd. For Found C, 50.56; H, 6.09; N, 2.39; S, 5.80 $C_{21}H_{24}O_{13}N_3S$; requires; C, 50.40; H, 5.20; N, 2.80; S, 5.40%]).

- **Synthesis of 1-hepta-O-acetyl-β-D-Maltosyl-5-p-toludine -4-dithiobiuret**

Yield72.8(%); Mp.84^{0}C;$[\alpha]_D^{32}$+133 (0.1, in $CHCl_3$);R*f* (Hexane:EtOAC)(1:1)0.80;**IR (KBr)cm- 1**:ν 3000-3292 (Ar-H)str ,1755 (C=O)str, 1543(C=N) str, , 1425 (C-N)str, 927(char. of glucopyranosyl ring), 758 (C=S) str. **^{1}HNMR (CDCl3)ppm:** 7.46-6.32 (m,8H, Ar-H), 5.57-3.87 (m, 7H, glucosyl-H), 2.31-2.01 (m, 12H,OAc),. **MS**(m/z) : 558 (M+),521, 408, 331, 263, 261, 169, 108.(Anal.Calcd. For Found C, 50.56; H, 5.54; N, 2.39; S, 5.27 $C_{21}H_{26}O_{11}N_3S$; requires; C, 50.30; H, 5.09; N, 2.80; S, 5.10%).

- **Synthesis of 1-hepta-O-acetyl-β-D-maltosyl-5-*p*-Cl-aniline-dithiobiurtes**

Yield 80 (%); Mp.145-150^{0}C;$[\alpha]_D^{32}$155.19(0.1, in $CHCl_3$);R*f* (Hexane:EtOAC)(1:1)0.87 **IR (KBr)cm- 1**:ν 3000-3292 (Ar-H)str ,1755 (C=O)str, 1543(C=N) str, , 1425 (C-N)str, 927(char. of glucopyranosyl ring), 758 (C=S) str.. **^{1}HNMR (CDCl3)ppm:** 7.46-6.32 (m,8H, Ar-H), 5.57-5.59 (m, 14H, lactosyl-H), 2.31-2.01 (m, 12H,OAc),.. **MS**(m/z) : 577 (M+),521, 408, 331, 263, 261, 169, 108.(Anal.Calcd. For Found C, 51.56; H, 5.89; N, 2.64; S; 5.78, $C_{20}H_{23}O_{11}N_3SCl$; requires; C, 52.17; H, 5.17; N, 2.89; S,5.62%%).

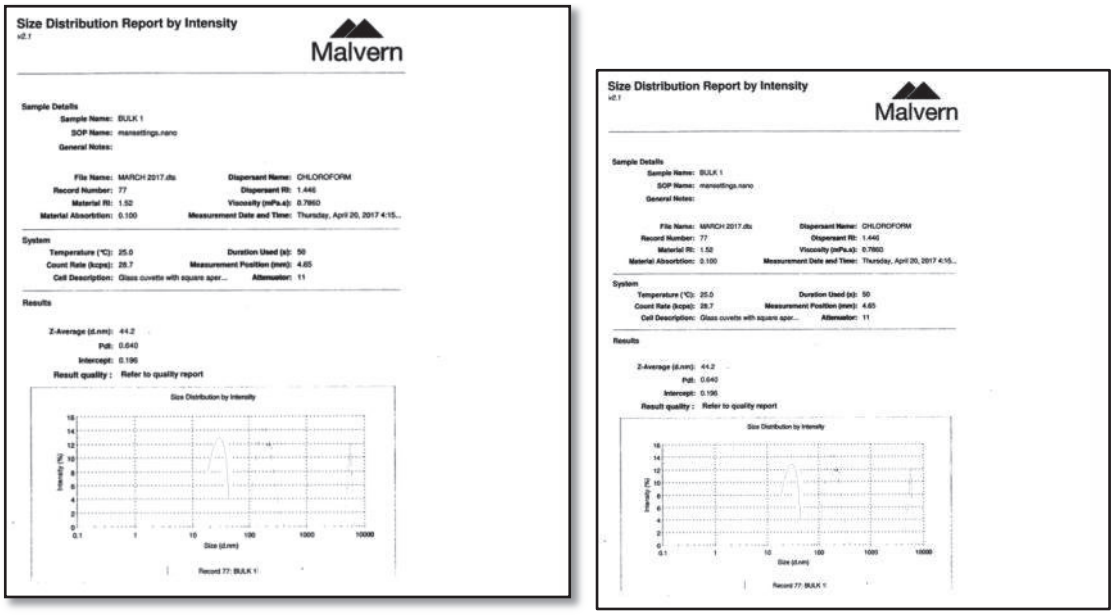
Preparation of Nanoparticles of hepta-O-acetyl-β-D-maltosyl-4-amino benzoic acid-4-dithiobiurets:

Take about 1 gm of hepta-O-acetyl-β-D-maltosyl-4-amino benzoic acid-4-dithiobiurets and dissolve it completely in the 50ml of solvent in 250 ml beaker. Now put this beaker in sonicator. The highly penetrating acoustic waves are passed through mixture, which create high pressure bubbles in the beaker due to which breakdown of the bulk material is takes place and desired sized nanoparticles are formed. The size determination of nanoparticlesis done by the X-ray diffraction studies

Characterization of Nanoparticles:

1. Characterization using UV-Spectrophotometer: Single Beam UV-Spectrophotometer with software BI/CI/SP/SB-S-03 of Bio Era make. The UV-Visible Spectroscopy reveals the formation of Nanoparticles Characterization of Nanoparticles was done using visible Spectrophotometer by using model by showing different absorption those from bulk material.

2. Size determination of hepta-O-acetyl-β-D-maltosyl-4-amino benzoic acid-4-dithiobiurets. Nanoparticles by X-ray Diffraction studies: From the X-ray diffraction it comes to know that size of nano **hepta-O-acetyl-β-D-maltosyl-4-amino benzoic acid-4-dithiobiurets** is 44.2 nm.



Antimicrobial activity comparison:

All the compounds have been screened for antibacterial activity using cup plate agar diffusion methodby measuring the inhibition zone in mm. The compounds were taken at a concentration of 1 mg/ ml using dimethyl sulphoxide as **solvent**.Amikacin (100ůg/ml) was used as a standard for antibacterial activity. The compounds were screened for antibacterial activity against *Escherichia coli, Staphylococcus aureus, S. typhi, and P. vulgaris* in nutrient agar medium.

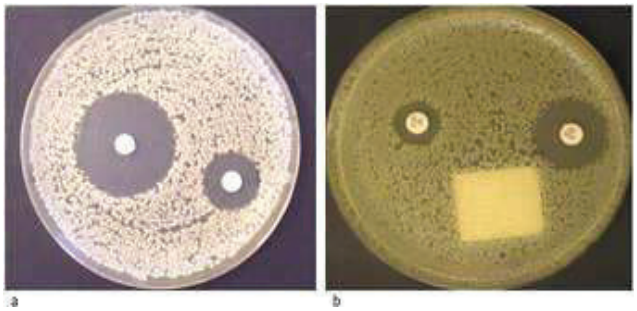


Table- 2 Antimicrobial activity of compounds

Antimicrobials	Bulk (5a)	Nanoparticles (6a)	Bulk (5b)	Nanoparticles (6b)	Bulk (5c)	Nanoparticles (6c)
E.coli	12	13	11	15	12	16
S.aureus	11	14	12	17	14	17
S.typhi	13	12	11	14	11	19
P.vulgaris	12	14	13	15	13	13
Amikacin	11	22	10	19	14	17
Clandamycine	10	15	12	13	12	14
DMSO	36	27	16	24	22	24

*including the well diameter of 8mm.**zone of inhibition in mm(15or less)resistance,(16- 20mm)moderate and (more than 20mm)sensitive.

Table No.3:- Characterization data of synthesis of 1-hepta-O-acetyl-β-D-maltosyl-5-aryl-4-dithiobiurets

Sr. No.	Aryl dithiobiurets	1-hepta-O-acetyl-β-D-lactosyl-5-aryl-4-dithiobiurets	M.P. (^{0}C)	% yield	Optical Rotation $[\alpha]_D^{32}$	R_f value
1	4-toludine	1-hepta-O-acetyl-β-D-lactosyl-5-p-toludine-4-dithiobiurtes	84	72.80	$[\alpha]_D^{32}$ = +133.94° (c, 0.373 in chloroform).	0.80
2	4-Cl-aniline	1-hepta-O-acetyl-β-D-	145 –	80.50	$[\alpha]_D^{32}$ = + 155.19°	0.87

		lactosyl-5-p-chloro-aniline-4-dithiobiuret	150		(c, 0.386 in chloroform).	
3	4-amino benzoic acid	1-hepta-O-acetyl-β-D-lactosyl-5-p-amino benzoic acid-4-dithiobiuret	135	71.60	$[\alpha]_D^{32} = +242.42°$ (c, 0.333 in chloroform).	0.59

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