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FROM THE EDITOR'S DESK....

The field of glycobiology is expanding rapidly with the development of numerous new, imaginative and efficient syntheses which provide further insight into structures and biological interactions of glycoconjugates which is fuelled by recent technological advances in molecular and structural biology, protein chemistry and analytical biochemistry. This new knowledge is being exploited industrially to produce novel carbohydrates for use in pharmaceutical, food and agricultural applications. In biology and medicine, oligosaccharides play a central role in immuno-stimulation, cancer or allergic responses. Glycoscience is a very instructive example of how one common topic of interest stimulates both chemistry and biology to collectively open scientific frontiers.

Recent Advances in Carbohydrate Bioengineering provides researchers and postgraduate students with a unique source of information on the latest advances in this exciting area. From a chemical standpoint, carbohydrates are ornery critters. They're complicated and hard to control, but recent advances show that researchers continue to make considerable progress in addressing the challenges that carbohydrates pose.

Chemists have made great strides in the chemical and enzymatic synthesis of complex oligosaccharides, and these compounds are now being used to make microarrays, which are important tools to study carbohydrate involvement in a large number of biological processes. Researchers are beginning to provide an understanding of the molecular details of carbohydrate-protein interactions. And we are starting to learn how this combined knowledge can be exploited in drug and vaccine design.

Carbohydrate microarrays, in which tens or hundreds of different sugars are bound noncovalently or bonded covalently in small spots on solid surfaces, have been under active development for a few years and are beginning to have broad use in research. The arrays are used to screen libraries of biological compounds, cell extracts, and other samples to assess the carbohydrate-binding properties of their constituents. Application areas include basic research, drug discovery, and diagnosis--as well as glycomics, the study of full complements of carbohydrates in cells, tissues, or organisms.

Scripps-based Consortium for Functional Glycomics (CFG) focuses on the effects of carbohydrate-protein interactions on cell communication. CFG focuses on glycan-binding proteins in mammals and in pathogens, the structures these proteins recognize, and the functional consequences of those recognition events.One of the classic challenges in the field of carbohydrate chemistry is that carbohydrate-based compounds and conjugates are notoriously hard to synthesize. Progress has continued on strategies to simplify and automate oligosaccharide synthesis and to facilitate the construction of larger and more complex glycopeptides and glycoproteins.

At the end, I would like to thank Sunita Hydrocolloids Private Ltd., Lucid Colloids Ltd and Hindustan Gum & Chemicals Ltd for financial support. I would like to urge the contemporary carbohydrate chemists to actively share any news item, information, event, scientific data, position available, prizes won, visit abroad, which you think should circulate in coming issues of CNL for young researchers working in the field of Carbohydrate chemistry and make the CNL more momentous.

Naveen K. Khare

ACCTI MEMBERS AT CARBO XXII, NIPER, CHANDIGARH ON DEC. 13, 2007

Presidential Address

Dear friends,

I feel privileged to welcome you all to the XXII Annual Convention of Carbohydrate Chemists and Technologists on behalf of the executive of ACCTI and my own behalf.

Today we have assembled here in the beautiful and prestigious campus of National Institute of Pharmaceutical Education and Research (NIPER) to interact and discuss the present Scenario in Carbohydrate research and technological needs of the industry. Distinguished Scientists, academicians, technologists, and industrialists, from all over the country and abroad have assembled here for this event. The stalwarts in their respective fields will make presentations in the form of key-note address, plenary lectures and invited lectures while research scholars will be presenting their research work as oral and poster presentations.

Since the last fifty years, India has been a developing country. 500 members of TIFAC (Technology information, forecasting and Assessment Council) have given thought to what should be the next vision of India. How do we transform a developing country into a developed country in the next 20 years? Five important areas have been identified to transform India- education and healthcare, agriculture, information and communication, infrastructure and critical technology.

The vision outlined could be achieved only by the brilliance and dedication of the research Scientists and Technologists. However it's a matter of concern that a country of over a billion people produces just about 5000 Ph.D's in Science annually. It is desirable to clear the cobwebs in our 250 Science Universities and 1500 research units. While the quality of dissertations may be debatable but I don't see any reason why our annual output of Ph.D's cannot be 4 to 5 times from the existing level. The present tendency to promote national laboratories at the expense of universities will not help the cause of the research. Both have distinct roles to play which need to be synergized.

India may be riding a sunbeam of unprecedented economic boom, but the country is facing a darkening environmental gloom. A blanket of smog hanging over the subcontinent is cutting down the sunlight. A study by the Indian Institute of Tropical Metrology in Pune goes on to say that India is getting about 5% less sunlight than that it did 20 years ago. A study reported in the New Scientist found that the amount of solar radiation reaching India's land mass dropped on average by 0.86 watts per square meter each year. Smog resulting from industrial activity, vehicular pollution, biomass burning and dust storms is increasing Aerosol Optical Depth (AOD) (which is the optical depth due to extinction by the aerosol component of the atmosphere) which results in less sunshine and because India is on steep industrialization and developmental curve, the AOD is only increasing and sunshine lessening.

India must now grasp the nettle and take initiatives to leap frog into clean technology. Investing in clean development pays financial dividends, too, via the carbon credits exchange market, a mechanisms recommended by UN's Kyoto Protocol to encourage rich countries invest in clean development initiatives in developing countries that emit less. An action plan must look beyond the immediate and focus on how India could shift to low carbon economic growth. To become global powerhouse and remain competitive, industry need to cultivate innovations in product development and processes, technologies and business model.

There is a tremendous challenge before the Carbohydrate chemists and Technologists to develop green technologies to utilize Carbohydrate biomass namely cellulose, hemicelluloses, starch etc for profitable processing. We have to adopt more imaginative ways to produce our target molecules with minimum adverse impact on the environment. Albert Szent Gyorgi, US Biochemist has rightly said “Research is to think what nobody else has thought.'

Since 1984, ACCTI has provided unique important platform for the growth and advancement of Carbohydrate Research in India by bringing together Scientists and Technologists from academic fields as well as industries to share their research results and exchange ideas and views. In the attaractive campus of NIPER we will be intellectually exposed for three days to different sessions where we shall be discussing on synthesis of oligosaccharides, Carbohydrate vaccines, glycocongugates, carbohydrate based drugs, structure of polysaccharides and their application in food and nutrition etc.

It is hoped with co-operation of all the delegates, XXII Carbo will be a great success.

Thankyou all

P.L.Soni

INVITATION for CARBO XXIII

The organizing committee takes pleasure in inviting you to participate in XXIII Carbohydrate Conference to be held at Bhavnagar University, Bhavnagar, Gujarat on December 3-5, 2008 in collaboration with Association of Carbohydrate Chemists and Technologists, India (ACCTI). The Conference will comprise of Plenary lectures, Invited lectures, Oral presentations as well as Poster presentations. **The conference will focus on the recent developments in the field of carbohydrate research with emphasis on the chemistry, biology and various other aspects related to industrial applications of carbohydrates. The conference will bring scientists, technologists, industrialists, educationalists and researchers on a common platform to discuss and exchange ideas on recent developments of the field. We look forward to see you there in CARBO XXIII.**

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Small-Molecule Galectin Inhibitors

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The galectins

The galectin family of β-galactoside-binding proteins have been ascribed importance in a wide range of biological mechanisms[1] For example, intracellular trafficking,[2] cell signaling[3-6] apoptosis,[7] and cell adhesion[8] are regulated by galectin activities. These galectin activities are observed as effects on the organism level in inflammation,[9] immunity,[10] and cancer progression.[11] Deciphering of galectin mechanistic pathways on a molecular level has accelerated during the last decade. Important recent investigations has mapped key galectin functions, such as the discoveries that different cell surface protein glycosylation patterns on different regulatory T-cells control galectin-1-binding and subsequent T-cell apoptosis,[3] that galectin-8 orchestrates intracellular targeting,[12,13] and that galectin-3-induced lattice formation with branched N-glycans regulates cell surface receptor localization.[4-6]. Furthermore, raft-independent apical sorting of proteins is regulated via galectin-3-controlled intracellular glycan-dependent clustering.[2] More recently, it was demonstrated that CD8-TCR co-localization was abolished by galectin-TCR lattice formation, which conferred anergy in tumor-infiltrating CD8+ lymphocytes.[14] All these observations lead to the conclusion that galectins are potential targets for novel anti-cancer and anti-inflammatory compounds. Hence, discovery of novel selective and potent galectin inhibitors is indeed desirable.[15,16]

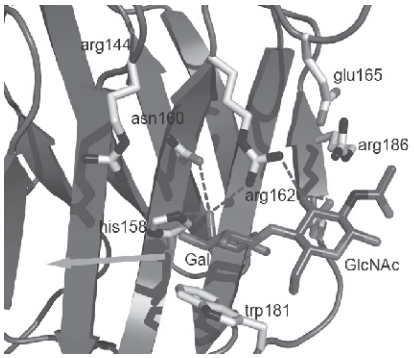
Inhibition strategies

A number of strategies for inhibiting the function of the galectins have been reported. These strategies are small-molecule carbohydrate inhibitors (synthetic and natural), dendrimers, small-peptide, anti-bodies, anti-sense nucleotides (ODN and siRNA), and dominant negative galectin-constructs.[16] Natural saccharides such as galactose, lactose and N-acetyllactosamine have been used both in vitro and in vivo treatment. The saccharides can be seen as small fragments of natural glycans and they likely act by binding competitively with natural ligands to galectins thus disrupting e.g. galectin-glycoprotein lattice formation. Dendrimers against galectins have, thus far, been decorated with natural saccharides and interact similarly as natural saccharides but make use of the affinity-enhancing glycoside clustering effect. A small peptide that inhibits galectin-3 has been reported.[17] Anti-galectin antibodies have been reported[18] to inhibit tumor cell aggregation and adhesion thus preventing metastasis. Anti- sense oligodeoxynucleotides (ODN) and anti-sense interfering RNA (siRNA) have been reported in in vitro and in vivo treatment of glioma and glioblastoma models.[19] A dominant negative galectin construct has been used in a human breast cancer mouse model.[20] In this study, an N-truncated galectin-3 construct, i.e. the galectin-3 terminus (Gal-3C) that contains the CRD, was used to competitively inhibit endogenous galectin-3. Since Gal-3C cannot multimerize due to the lack of N- terminus, it binds to natural ligands but does not confer any further function or signaling. Finally, synthetic, small-molecule inhibitors bind in competition with endogenous ligands to prevent normal galectin function. The strength of synthetic small-molecules is that they can be made chemically and enzymatically more resistant, thus being the most promising inhibition strategy for oral administration. Synthetic small-molecules can be made more hydrophobic than other inhibitors, allowing improved bioavailability. Importantly, they can potentially be made higher-affinity than natural ligands (and also natural small-molecule carbohydrate inhibitors) thus requiring smaller amounts to compete successfully with the natural ligands. Herein, we present an overview of our recent progress in the design and synthesis of small-molecule galectin inhibitors.

Small-molecule inhibitor design and synthesis

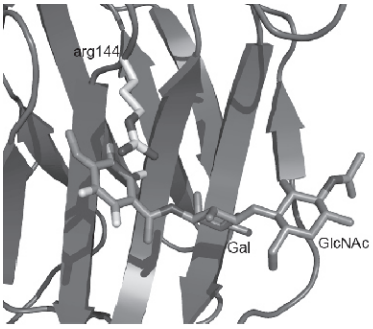
The development of galectin inhibitors has been helped immensely by the X-ray structure of galectin-3 in complex with LacNAc.[21] In the X-ray structure, the carbohydrate binding groove can be seen extending beyond the 3'-position of the LacNAc into two branches, giving the first idea as to affinity-enhancing derivatizations (Figure 1).

Figure 1: X-ray structure of galectin-3 co-crystallized with LacNAc. An extended binding pocket is indicated by arrows.



The observation of these extended binding sites initiated research to find high affinity 3'-LacNAc derivatives, subsequently 3'-benzamido-LacNAc derivatives were the first sub-micromolar affinity synthetic galectin-3 inhibitors reported.[22] Aromatic 3'-LacNAc amides (Scheme 1, structure **1**) turned out to bind in the high nano-molar range. The amide confers improved affinity and may also confer improved hydrolytic and enzymatic stability vs e.g. the corresponding esters. An X-ray crystal structure of galectin-3 co-crystallized with one 3'-benzamido-LacNAc derivative[23] revealed the following: an arginine (Arg144) in the extended binding site moved over 3Å to create a cavity for the aromatic moiety and to simultaneously sandwich it (Figure 2). The major affinity increase by the benzamido group probably comes from surface complementarity with its hydrophobic interactions with the bulk of the protein, i.e. affinity driven largely by desolvation effects. However, a large contribution is also believed to come from the π-cation interaction[24] with the guandinium group.

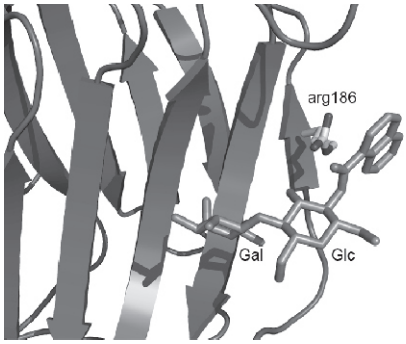
Figure 2: X-ray structure of galectin-3 co-crystallized with a 3'-benzamido-LacNAc derivative.**25**



Structurally simple inhibitors targeting another arginine side chain in galectin-3 (Arg186) and the corresponding Arg74, Arg75, and Arg 87 in galectin-1, 7, and 9N, were synthesized by lactose O2 benzoylations (Scheme 1, structure **2**). The lactose 2-O-benzoates were hypothesized to stack face-to-face to these Arg side-chains to form cation-π interaction (Figure 3) and indeed low μM inhibitors that were 50-200 times superior to lactose were identified.[25]

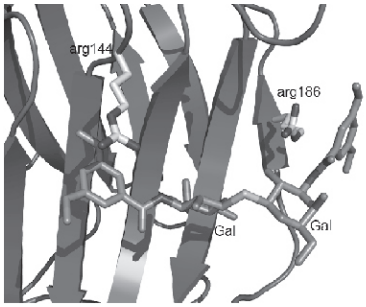
The concept of placing aromatic moieties onto Arg186 was successfully combined with the Arg144-interacting 3-benzamido-galactoside scaffold to provide 3,3'-di-benzamido-thiodigalactosides (Scheme 1, structure **3**) that simultaneously interact with two arginine side chains.[26] In the 3,3'-di-benzamido-thiodigalactosides, one of the galactose moieties corresponds to the galactose unit of the natural LacNAc ligand, while the second galactose moiety mimics the GlcNAc unit of LacNAc. The binding thermodynamics[27] are improved both by forming an entropically favoured C2-symmetrical inhibitor and by forming a second π-cation interaction, this time with Arg186 (Figure 4). The creation of double arginine-arene interactions leads to inhibitors that bind Gal-3 with a K_d down to 33 nM.

Figure 3. Benzoylation of lactose O2 provided efficient inhibitors of galectins. The O2-benzoates stacked onto conserved Arg side-chains, as here exemplified with Arg186 of galectin-3

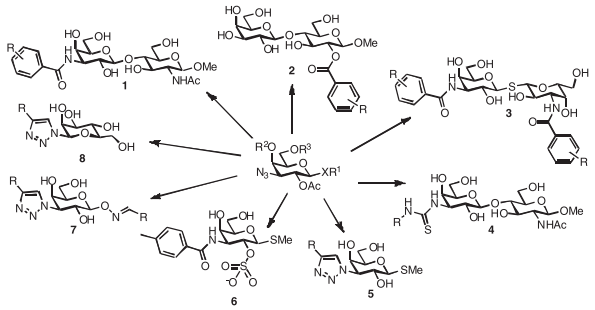


In lieu of the galactose C3-benzamides, the corresponding thiourea and 1,4-substituted triazole derivatives have been proven to be potent galectin inhibitors. Conversion of a 3'-amino LacNAc derivative into an isothiocyanate, followed by amine addition, was used to create a collection of 3'-thioureido-LacNAc derivatives (Scheme 1, structure **4**) that were demonstrated to inhibit galectin-7 and 9N with selectivity.[28] Installation of 1,4-triazoles at galactose C3 was readily done with a 3-azido-3-deoxy-β-D-galactoside and a suitable terminal alkyne using the Huisgen 1,3-dipolar cycloaddition which, under Cu(I) catalysis,[29-31] preferentially forms the 1,4-cycloadduct (Scheme 1, structure **5**). The galactose C3-triazoles were demonstrated to be inhibitors of galectin-3[32] with efficiencies equaling those of the corresponding aromatic galactose C3-amides.

Figure 4. Low nM-affinities of 3,3'-di-benzamido-thiodigalactosides for galectin-3 is conferred by double arginine-benzamide interactions.

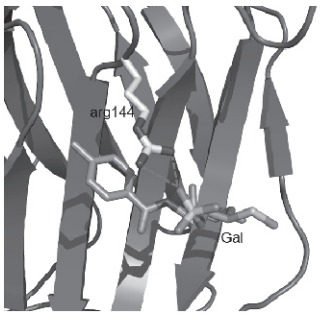


Hence, various C3-derivatizations on galactoside derivatives enabled affinity-enhancing interactions with extended galectin cavities near this galactose position. Other regions of the galectin CRD that may be suitable to target with



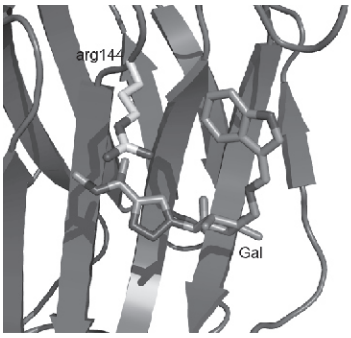
Scheme 1. Galectin inhibitors derived from 3-azido-3-deoxy-galactoside derivatives. (X=O or S, R^1=alkyl or aryl, R^2,R^3=OAc or benzylidene.) structural elements added to galactose core scaffold can be identified by inspection of galectin crystal structures. While the ?-face of galactose resides on the plane of a trp side-chain, the ?-face of galactose is “zipped” up by forming hydrogen bonds the protein arginine side chains. As all galectins exploit 1-3 basic amino acid (Arg or His) to form such polar interaction with galactose, it appeared reasonable to assume that electron-rich substituents added to galactose may engage in strong interactions with his or arg side chains. The HO4 and HO6 of galactose are engaged in key polar interactions with all galectins, while galactose HO2 is not. Based on this notion, a 3-azido-3-deoxy-β-D-galactoside was derivatized at O2 with electron-rich substituents (Scheme 1, structures **6**) and it was proved that this resulted in enhanced binding to galectin-3. The most promising O2 substituent was a sulfate and molecular modeling suggested that the sulfate indeed interacts with Arg144 of this galectin. Hence, binding was enhanced due to an added salt-bridges involving the galactose-2-O-sulfate and Arg144 side chains (Figure 5).[33]

Figure 5. A galactose 2-O-sulfate forms a salt bridge with Arg144 of galectin-3.



A complementary strategy has been to attach Glc/GlcNAc-mimicking aglycons to ?-D-galactose. Galactosyl oximes, where anomeric aromatic oximes mimic Glc/GlcNAc, were demonstrated to provide efficient monosaccharide inhibitors of galectin-3,[34] Properly trisubstituted phenyl aglycons of 1-thio-?-D-galactosides were found to mimic Glc binding properties of galectin-7 and were comparatively efficient inhibitors.[35] The galactosyl oximes and the phenyl 1-thio-?-D-galactoside inhibitors are synthetically simpler than thiodigalactoside-based inhibitors and possibly more stable in vivo than natural disaccharide-based (i.e. lactose, LacNAc). Consequently, they are from this perspective more promising leads for drug development. The galactosyl oximes could be combined with C3-triazoles earlier identified as strongly galectin-3-binding moieties to provide monosaccharides (3-triazolyl-galactosyl oximes, e.g. **4**, (Scheme 1, structure **7** and Figure 6) that inhibited this galectin with K_d as low as 11 μM (unpublished).

Figure 6. A 3-triazolyl-galactosyl oxime pinches Arg144 of galectin-3, which results in high affinity.



Finally, other pyranosides having at least one 1,2-cis-diol may be explored as galactose mimics. Within this context, we developed triazolyl ?-D-mannopyranosides as galectin inhibitors in which the anomeric triazolyl moiety mimicked a galactose C3-triazole moiety and mannose O2 mimicked galactose O4.[36] Furthermore, the ?-face of galectin-bound galactosides is directed towards a line of Arg and/or His side chains, which laid the basis for designing and synthesising ?-D-talopyranosides as galectin inhibitors. The inverted configuration at talose C2, as compared to galactose C2, was hypothesized to direct O2, as well as O2 substituents towards the line of Arg and/or His side chains. Indeed, taloside derivatives were found to inhibit galectin-3, 4C, and 8N and the two later galectins in fact preferred the talose of the galactose configuration.[37] Hence, talopyranose is a more promising scaffold than galactopyranose for the development of inhibitors targeting galectin-4 and 8.

Outlook

It is commonly stated as a general truth that monovalent carbohydrate-protein interactions are weak and that lectins therefore make poor drug targets. However, galectins typically bind natural disaccharide ligands with low μM affinity, or in some cases even nM affinity as for galectin-8N binding sialyllactose,[12] and thus make an exception. Indeed, we have through combination of monosaccharide mimicking and appending non-carbohydrate structures to saccharide scaffold proved that it is possible to develop small-molecule galectin inhibitors with low nM affinities required for drug leads. Challenges that remain to be tackled are improving ADME properties of the compounds, in particular bioavailability and stability to in vivo degradation and clearance. It can be expected that further structural modification of our galectin inhibitors can address these challenges and that they eventually will be developed into galectin-targeting drugs that fight tumor progression and inflammatory conditions via novel mechanisms.

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Biofuels and The Plant Cell Wall: Opportunities and Challenges for Synthetic Carbohydrate Chemistry

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Abstract - With the increasing need to phase out fossil fuels in favour of sustainable feedstocks, we are challenged with how to capitalise on renewable natural resources. This article highlights some of the areas where there is a need for input from synthetic and analytical carbohydrate chemistry.

Major initiatives in the United States, in particular, are targeting the transition from an oil-based economy to renewable feedstocks capable of supporting energy and bulk chemical needs.[1,2] At the heart of such programs is the need to identify, breed or (genetically) engineer new plants for biomass production *en route* to liquid fuel (e.g. bioethanol) and platform chemical (e.g. glycerol) production. For the purposes of this article, we shall focus on carbohydrates,[3] whilst acknowledging that lignin utilisation also presents major challenges.[4] Plants differ enormously in their chemical composition, and even in their specific carbohydrate content, both of which have implications for the processibility. Pauly and Keegstra note[3] that "Plant cell walls represent the most abundant renewable resource on this planet yet only 2% of this resource is currently used by humans. Hence, research into the feasibility of using plant cell walls in the production of cost-effective biofuels is desirable. The main bottleneck for using wall materials is the recalcitrance of walls to efficient degradation into fermentable sugars. Manipulation of the wall polysaccharide biosynthetic machinery or addition of wall structure-altering agents should make it possible to tailor wall composition and architecture to enhance sugar yields upon wall digestion for biofuel fermentation. Study of the biosynthetic machinery and its regulation is still in its infancy and represents a major scientific and technical research challenge."

The challenges associated with delineating plant cell wall biosynthetic pathways is also apparent more broadly in 'glycobiology'.[5] The myriad of proposed biological functions for carbohydrates is daunting.[6] This complex situation has been helped little to date by the range of genome sequencing programs now complete: even with the model plant *Arabidopsis thaliana*, the gene count runs to 25498 (of the same order as man!).[7] Perhaps 6% of the Arabidopsis genome (~1525 genes) can be assigned a function in some aspect of carbohydrate (bio)chemistry; genes encoding **379 glycosidases and 414 glycosyltransferases have been identified,**[8] although to date very few of these functional assignments have been verified experimentally. Roughly **420 genes have been assigned probable roles in cell wall polymer formation, including more than 60 genes for glycosyltransferases.**[7] This situation is symptomatic of glycobiology in general: informatics tools have proved invaluable in identifying which class of enzymes (glycosidases vs glycosyltransferases, for instance), or even which family/clade a given enzyme belongs to, but generally one cannot predict enzyme substrate specificity from gene sequence. Even with a protein crystal structure in hand, predicting substrate specificity is still fraught with problems, although the situation is improving.[9,10]

In the context of appreciating the biosynthesis and function of the cell wall 'system',[11] the need for new 'technologies' is evident.[12] The root cause of many of the issues faced in the carbohydrate arena lies in the fact that, in contrast to nucleic acids and proteins (i.e. DNA codes for RNA codes for protein), oligosaccharide structures are not template-encoded (i.e. one cannot [yet] read gene sequence and predict oligosaccharide sequence). On top of that, there is a complexity issue: whilst **5 molecules of alanine can be coupled together to form only a single linear peptide, and this polypeptide can be made on a commercial peptide synthesiser, combining 5 molecule of glucose can give rise to 17872 different structures (allowing for stereo- and regio-isomers). Considering 5 different building blocks, 120 pentapeptides and 2144640 pentasaccharides are conceivable.**[13] **With no automated oligosaccharide synthesiser commercially available at present, and with no straightforward equivalent of the polymerase chain**

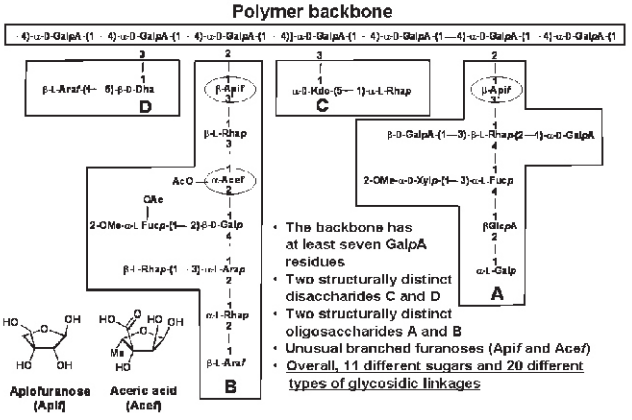


Figure 1: The primary structure of Rhamnogalacturonan II (RG-II), showing the backbone and four major side-chains (A-D) and the unusual branched furanoses apiofuranose and aceric acid.

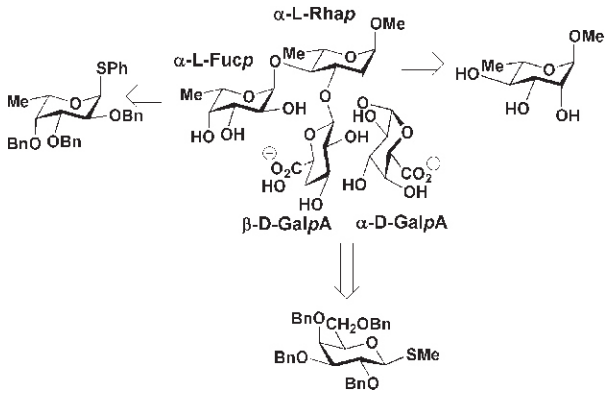
reaction, site-directed mutagenesis or Edman sequencing, confirming the composition/structure of oligosaccharides and their subsequent chemical synthesis remains a formidable challenge. A recent informatics analysis of the diversity of mammalian carbohydrate structures identifies that just 11 monosaccharide connections account for >75% of all linkages found in oligosacharides.[14] Thus, the number of structural combinations found in mammalian 'glycospace' is much smaller than had been expected. However, in the plant kingdom, things are on an altogether more complex scale: the pectic oligosaccharide rhamnogalacturonan II (RG-II; Figure 1) alone is composed of at least 12 different types of sugar residue linked together by more than 20 different glycosidic linkages.[15] Rather oddly, this structure is conserved throughout higher plants. Whilst advances in understanding the biosynthesis of pectins continue to been made, much remains to be learned.[16,17]

In order to illustrate some of the chemical challenges in plant cell wall glycoscience, we will look specifically at RG-II. From a biological perspective, this complex, branched structure is central to plant morphology: mutants in RG-II biosynthesis are

severely compromised in their ability to grow and maintain an upright stature[18] In addition, from a synthetic chemistry point of view the range of glycosidic linkages (Figure 1) presents a challenge for both method development and target synthesis. Tieing synthetic chemistry to plant physiology, RG-II is thought to be unique in its ability to (reversibly) self-assemble through borate complexation, which provides a means of effecting polysaccharide chain cross-linking.[17,18] Allowing for the need for restructuring the cell wall as a function of cell growth and division, this complexation process must be dynamic and tightly regulated. At this stage it is unclear if the formation and cleavage of RG-II borate esters is enzyme-catalysed or if it a wholly chemical process, governed by the predisposition of a key monosaccharide unit (D-apiose) to complex borate. Perhaps this process constitutes an example of naturally occurring supramolecular chemistry controlled by environmental factors (such as pH or metal ion concentration).

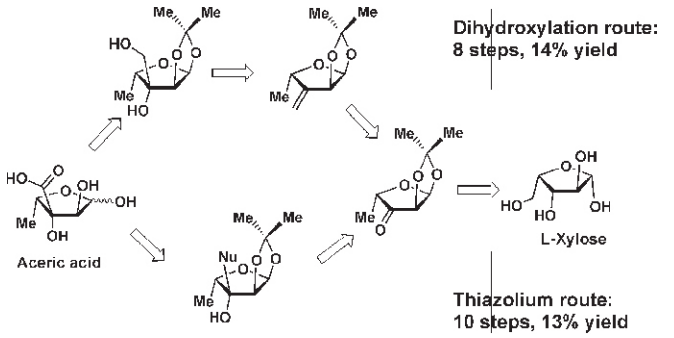
Understanding the biosynthesis and borate complexation of RG-II would benefit enormously from synthetic oligosaccharide fragments. A number of labs have reported syntheses of fragments of side-chains A and B.[19-24] In our work, the synthesis of the side-chain A branched tetrasaccharide first required the development of practical methods for the synthesis of thioglycoside building blocks.[25] The overall synthetic strategy took advantage of the fact that this tetrasaccharide does not contain a primary alcohol, which allowed the allowed the late-stage oxidation of the galactose units to uronic acids (Figure 2).[21]

Figure 2: Strategy for the synthesis of a branched tetrasaccharide component of RG-II side-chain A



Glycosylation methodology continues to advance rapidly, and in so doing it highlights just how longwinded monosaccharide building block chemistry can be. Again in the context of RG-II synthesis, a classical approach to the preparation of the rare branched furanose aceric acid demonstrates this inefficiency (Figure 3).[26] Whilst the routes shown make use of chiral pool starting material, the *de novo* synthesis of partially protected monosaccharides by carbon backbone extension (aldol chemistry) has been explored.[27,28] In addition, exploiting contemporary organocatalysis options, the total synthesis of monosaccharides from 2-carbon aldehydes has also been reported.[29] These later approaches provide rapid and direct access to partially protected sugar building blocks, which are more difficult to prepare from carbohydrate precursors. Perhaps in future carbohydrates will *not* in fact serve as the key precursors for carbohydrate chemistry!

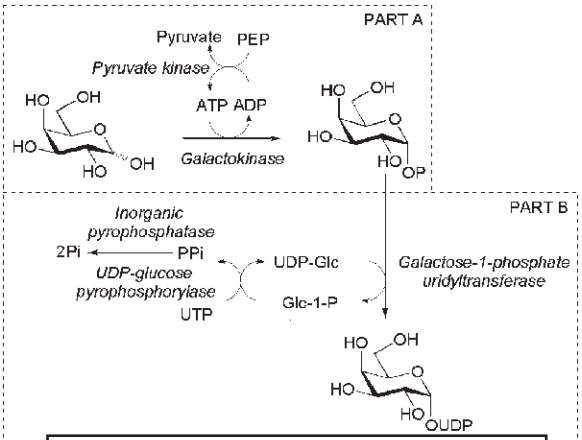
Figure 3: Synthetic routes to the novel branched monosaccharide aceric acid



From a biosynthesis perspective, having synthetic oligosaccharides in hand leaves availability of sugar-nucleotides[30] as a key challenge in establishing glycosyltransferase assays. Here one can exploit that natural background chemical competence of enzyme to utilise non-natural substrates at low efficiency (Figure 4).[31]

With donor and acceptor biosynthetic building blocks in hand, one then need to consider assay methods. The development of high through-put carbohydrate array-based approaches is gaining momentum,[12,32] with fluorescence,[33] SPR,[34] and mass spectrometry[35,36] read-outs being explored. Carbohydrate microarrays are also beginning to be used to assays plant cell wall glycosyltransferases.[37]

Figure 4: Flexible enzymatic synthesis of UDP-sugars



modified position	substituent[a]	Yield (%)
-	D-Galactose	98
C-2	-H	98
C-2	-F	97
C-2	$-NH_2$	95
C-2	-NHAc	19
C-2	$-N_3$	-
C-3	-F	64
C-3	$-N_3$	-
C-5	$-CH_3$ (D-Fucose)	57
C-5	$-CH_2F$	37
C-5	-H (L-Arabinose)	47

In summary, the biofuels agenda impacts on the big picture of societal and environmental issues. However, it also presents opportunities and challenges for the carbohydrate chemist, some of which are highlighted herein.

Acknowledgements
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Engineering D-Glucose and D-Galactose to New Antimycobacterial Agents

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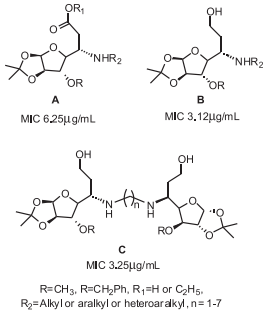
An increase in the global burden of tuberculosis with the worldwide mortality rate of 23% is a major cause of concern in the socioeconomic and health sectors. The synergy of this disease with HIV infection and the emergence of MDR tuberculosis (TB) pose a threatening global challenge particularly in the developing countries. Although a number of lead molecules exist today to develop new drugs, no new chemical entity has emerged for clinical use over the last 45 years for the treatment of this disease.[1] Therefore; there is an urgent need to develop new drugs, acting through a novel mechanism of action for the chemotherapy of TB.

Among several targets known to develop a new antitubercular agents, mycobacterial cell wall is an unique target in the sense that it is absent in human host and is also responsible for development of drug resistance. The latter is due to incredible thickness of the cell wall which imparts the permeability of the nutrients inside the cell wall and protects the organism from the immune system of the host. In fact this thick wall of the bacterium is one way responsible for a long duration of treatment of the disease. Mycolylated Arabinogalactan Peptido glycan complex (MAGP) highly glycosylated and constitute the major component of the cell wall. The cell wall

components are also implicated in pathogenesis and evading the host immune system.[1] In Central Drug Research Institute our group has initiated a programme on developing new antitubercular agents from simple sugars keeping in mind several components of cell wall and their biosynthetic enzymes. In an endeavor, we have synthesized β-glycosylated amino acids, esters and alcohols and engineered them into compounds possessing potent antitubercular activities as shown below.

The synthesis of glycosyl amino esters, acids and alcohols is described earlier[2] which is basically a Micahel addition of amines to glucose derivatized olefinic esters followed by further desired chemical engineering. The most active compound prototypes **A**, **B** and **C** are sketched below (Figure 1).

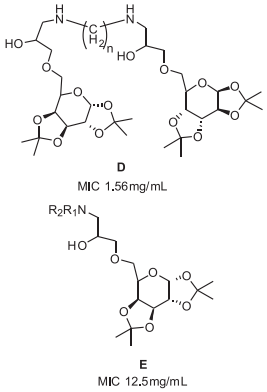
Figure 1: Prototypes displaying anti-tubercular activity



The diamine derivatives of xylofuranose derivatives **C** were the most potent compounds and they exhibit antitubercular activity even against MDR tuberculosis.[3]

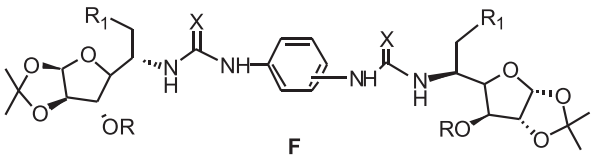
In another approach, aminoalkanol derivatives of galactopyranose derivatives **D** and **E** were prepared by oxirane ring opening of the appended epoxyalkyl derivatives of galactopyranose.[4] The amino alcohol shown below displayed MIC value 1.56µg/mL, comparable to ethambutol in vitro (**Figure 2**). The compound displayed in vitro activity against several MDR strains of M. tuberculosis. However, the compound could not protect the infected mice in vivo.

Figure 2: Galactopyranosyl amino alcohols



The amino esters, so obtained were manipulated to glycosyl acyclic and cyclic ureides and thioureides (**Figure 3**), which proved to be novel inhibitors of DNA ligase from M. tuberculosis and inhbited the mycobacterial growth also. Further, these prototypes were selective to Mycobacterium and nontoxic to human DNA Ligase.[5,6,7]

Figure 3: Glycosylated ureids and thioureids as inhibitors of mycobacterial DNA ligase

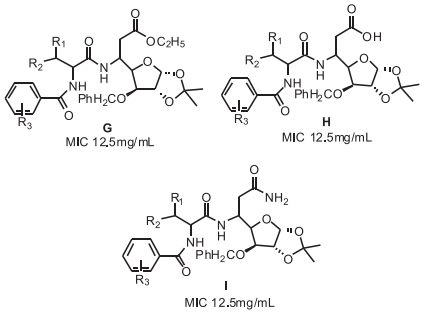


IC_{50} = 85.0 to 11.4 µM

R_1=$COOC_2H5$, CH_2OH, $COOH$,; X=O or S

Further, the glycosyl amino acid derivatives were used in combinatorial synthesis of novel series of glycoconjugates (**Figure 4**) which inhibited mycobacterial growth in vitro. Few of the selected compounds were effective against MDR strains of *M. tuberculosis*. The compounds were synthesized both on solid phase as well as via conventional solution phase synthesis.[8]

Figure 4: Combinatorial library of glycoconjugates



The compounds displayed activity against MDR tuberculosis. These compounds have potential for other bacterial diseases as well. The detailed investigation of this series is underway.

In conclusion a chemical engineering of simple sugars D-Glucose and D-Galactose have led to identification of new prototypes holding the promise towards the development of new chemotherapeutics. The new prototypes after suitable manipulative strategies may offer new leads for tuberculosis, a disease of national priority and global threat.

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Minutes of the Annual General Body Meeting-2007

The Annual General Body meeting of the Association of Carbohydrate Chemists and Technologists (India) was organized by the Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, on 13th December, 2007, at the auditorium. Thirty-two members of the Association attended the meeting. President, Dr. P. L. Soni, delivered the introductory speech. Dr. A. K. Sen, Secretary of the ACCT(I), then read out the minutes of the previous AGB meeting held during the XXIth Carbohydrate Conference which was organized by the Chemistry Department, Delhi University. The minutes were accepted unanimously: Proposed by Dr. Vasudeva Singh and Seconded by Dr. R. P. Tripathi.

Dr. A. K. Sen then described the previous years' activities of the Association. The meeting of the Executive Committee members was held on 12th December, 2006, in the evening where the EC members exchanged there views for the betterment of the activities of the Association.

The treasurer of the Association Dr. P. K. Gupta then presented the audited 'Statement of Accounts' of the ACCT(I), After a brief discussion, the 'Statement of Accounts' was accepted by the members. In view of the enhanced activities of the Association and also considering the increase in price index he requested members to consider increasing the membership fee. He also mentioned that the present membership fee has remained unchanged for the last six years. The learned members discussed the issue and felt that it is legitimate to increase the membership fees. The members decided that the new membership fees should be as follows: Life membership fee: Rs. 2000.00 for academicians & Rs. 4000.00 for persons from industry, Rs. 500.00 per year for ordinary membership, Rs 50,000.00 for Patrons, with effect from 01.01.08. It was proposed by Dr. Hasi Das and seconded by Dr. K. P. R. Kartha.

Dr. N. Khare, Hon. Editor of the Carbohydrate News Letter (CNL), then placed the 'Statement of Accounts' of CNL which was accepted unanimously; proposed by Dr. Vineet K Madan and seconded by Dr. V. Singh. The members thanked Prof. Naveen Khare for the excellent outcome of CNL-2007. On request of Prof. Khare, the members decided to appoint two Associate Editors. Both Dr. R. P. Tripathi and Dr. Balaram Mukhopadhyay kindly agreed to become the Associate Editors and were welcomed by the members. The CNL is currently published once a year on 'no loss no gain' basis. The publication of the CNL is partially sponsored by the ACCT(I) and also from the earnings from the advertisements. Since the cost of publication has increased, Prof. Khare proposed an increase in the rate of publications of the advertisements; Rs. 3000.00 for back cover page, Rs. 2500.00 for inside cover page, Rs. 2000.00 for full page. The proposal was accepted by the members and was seconded by Prof. D. Loganathan. The members also requested the industrial houses to come forward to sustain the CNL.

The current website of the Association is hosted in a fee Yahoo Geocities domain with a limited bandwidth. In view of the International Carbohydrate Conference, Dr. Asish Sen pointed out that the Association needs a website with its own domain name and higher bandwidth. After discussion the members requested Dr. Sen to explore the issue and a sum of Rs. 5000.00 was granted for the purpose. The members felt that a database of the member scientists and technologists should be available in the website for ready reference. Accordingly, Dr. K. P. R. Kartha was requested to design a suitable form and distribute it amongst the members for the construction of the database.

Dr. P. L. Soni then described the current position of the 'Trends in Carbohydrate Research' and the difficulties he is facing in launching the journal. The members appreciated his sincere effort. They also requested Dr. Soni to consider an e-journal. The members discussed the format of the journal and settled on two issues per year and that a general guideline as per Indian Journal of Chemistry, Sec. B. was to be followed. After some discussion the Editorial Board of the journal was constituted based on the expertise in area of research, and is as follows: Editor-in-Chief: Dr. P. L. Soni, Associate editors: Prof. G. Chauhan, Dr. Hasi Das, Dr. K. P. R. Kartha. Prof. Naveen Khare, Prof. D. Loganathan, Dr. Vineet Kumar Madan, Prof. N. K. Mathur, Prof. Balaram Mukhopadhyay, Prof. Ashok Prasad, Dr. Bimalendu Ray, Dr. Asish Kumar Sen, Dr. Vasudeva Singh, Dr. R. P. Tripathi, Prof. H. C. Trivedi. It was also decided that some eminent scientists from outside India will also be included as Associate Editors. The proposal was accepted by the members. It was proposed by Prof. H. C. Trivedi and seconded by Prof. B. Mukhopadhyay. The GB decided that from next (i.e. 2008) year ACCT(I) will sponsor a special lecture in the memory of the late Dr. H. C. Srivastava, Founder President of the Association. The orator will be honoured with a medal and a cash award of Rs. 10,000.00. The proposal was well received by the members and was unanimously approved. It was proposed by Prof. H. C. Trivedi and seconded by Prof. D. Loganathan. It was also decided by the members that the best person to deliver the first lecture will be Prof. N. K. Mathur, who kindly accepted.

Various other issues were also discussed in the meeting. Some of the members felt that ACCTI should institute a Fellow of ACCTI (FACCTI) commendation. This was agreed on principal. Dr. Sen proposed that the standard protocol of INSA be followed and that it would be most appropriate to launch this during the 25th year of ACCTI. In view of the increased participation of International scientists, the proposal for the change of name of the National Carbohydrate Conference to India International Carbohydrate Conference was not accepted by the members. The proposal to announce the name of all the co-workers with the name of the young scientist awardees was accepted.

It was decided that the XXIIIrd Carbohydrate Conference would be held at the Bhavnagar University, Gujarat. Prof. H. C. Trivedi, Vice-Chancellor, will take the responsibility. There were many contenders for the 24th and the 25th meeting including I.I.T. Mumbai. Dr. A. K. Sen suggested that the 25th conference should be held at Head Quarters of the Association at Dehradun. Dr. Soni promised to consider the matter. It was decided that the concerned Institutions should attend the next meeting with definite proposals, based on the merit of which the venue for the next two meetings would be finalized.

The meeting lasted for nearly one and an half hours and was concluded with a vote of thanks to the chair by the Jt. Secretary Prof. Naveen Khare.

Dr. A. K. Sen (Secretary)

Life Time Achievement Award

The Association of Carbohydrate Chemists and Technologists of India (ACCTI) is privileged to honour the most successful chemists, biologists and technologists in the country who are working in the field of Glycoscience. Recently, Mr. Nikunj Dhuldhoya of Lucid Hydrocolloids was awarded the Life Time Achievement award for the year 2007 at CARBO XXII held at NIPER, Mohali, Chandigarh in Dec. 2007.

Mr. Nikunj Dhuldhoya was born on 12th Nov. 1948 at Mumbai and has got B.Sc in 1969, M.Sc. in 1973 from UDCT, Mumbai. He is an examiner for the evaluation of Master's and Doctorate thesis in University of Mumbai. He started his carrier as a junior chemist in 1973 and has risen to Director R&D and Quality Assurance in Lucid Hydrocolloids.

He has developed many products by substitution reactions in sequential system from lab scale to commercial scale. The list of development is too big, however I would like to apprise the distinguished delegates with few only. These are Carboxyl methyl derivatives of Guar, starch and TKP. Carbooxylmethyl-hydroxyalkylguar, cholorohydroxypropyltrimethyl ammonium chloride derivative of guar. Hydroxyalkyl guar and tamarind. Very high and fast hydrating Guar.

He has also provided guidance for high quality and hygiene standards for partially hydrolysed Guar Gum manufactured at Taiyo-Lucid (Joint Venture with Japan) and also working as a technical Coordinator of Lucid Hydrocolloidscolloids, sponsored projects with UICT Mumbai, KMKC of Pharmacy, Mumbai and L.A.D college of Cosmetology, Nagpur. He has made many useful presentations to customers around the world for importance of products developed by him and their applications resulting into better image and prestige of the company as well as making a big business deal too.

This is the speech delivered by Mr. Nikunj Dhuldhoya after receiving the lifetime achievement award of ACCTI at NIPER, Chandigarh on Dec. 13, 2007.

Dear Dr. P.L.Soni-President ACCTI, Dr. A..K.Sen-Secretary-ACCTI, Dignitaries on Dias, Invited Guests from India and abroad, ACCTI-members, Students, Ladies and Gentlemen.

I am indeed deeply honored and touched today in receiving this prestigious life time achievement award from Association of carbohydrate chemists

and technologists of India and Lucid colloids limited. Please accept my sincere thanks.

When I joined Indian Gum industries as junior chemist I never thought that my 30 years of long association with the company would witness so many value added products of these natural gums. Whatever I could contribute in research and developments of new products, new methods of testing for better control of these products was mainly due to founder of this company late shri Chatrubhuj Gordhandas (Popularly known as Shri Kakubhai) in Giving able guidance in earlier time of my years and now continued by shri Uday C . Merchant. I learnt lot from the informations gathered from the ACCTI conferences, Basic high standard of education from UDCT, now known as UICT.

We have developed and catered products to many kinds of industries and still also continual improvements in products are achieved by adding values Thru research input. My sincere thanks to my team of research and development, quality assurance, production and marketing department. Also my Thanks to wife Yaksha for tolerating extra hours at labs.

I once again thank ACCTI and Lucid colloids. I am obliged to them in giving me pleasant memory for rest of my life.

Thank you all for the patience.

Hydrocolloids Efficient Rheology Control Additives

N.C. Dhuldhoya

Lucid Colloids Limited, Mumbai-400015

Rheology - An Introduction

Rheology is defined as "the study of the change in form and the flow of matter embracing elasticity, viscosity and plasticity". We concern ourselves with viscosity, further defined as "the internal friction of a fluid caused by molecular attraction, which makes it resist a tendency to flow."

Water is an invaluable solvent and vehicle but it is having certain deficiencies. It is, above all, watery. The exercise of rheological control over water is a significant challenge for formulators. Formulators are therefore forced to adjust water to suit their needs. Fortunately, this can be readily accomplished through the use of rheology modifiers.

Specific control of water is enabled by the careful application of one or more of the rheology modifiers available for use in aqueous compositions. Familiarity with the rheological nuances of a particular modifier can at times make the difference between an exceptional formulation and a routine one. What follows is an overview of the hydrocolloids based additives most commonly used to control water. The intent is to make the formulator sufficiently familiar with the fundamental nature of each of these materials, so as to facilitate proper selection.

Rheology Control Additives

Guar Gum

Description: Guar gum is a nonionic hydrocolloid obtained from the ground endosperm of the legume *Cyamopsis tetragonolobus*, an annual plant which grows mainly in arid and semi-arid regions. It is soluble in cold water and gives visually hazy, neutral pH solutions.

Rheology: Guar gum shows pseudoplastic or "shear thinning" behavior in solution. The degree of pseudoplasticity increases with concentration and molecular weight. Solutions of guar gum do not exhibit yield stress properties.

Compatibilities: Guar gum is compatible with most nonionic and anionic gums, featuring useful synergism with some microbial gums. It is soluble in salt solutions that contain up to 70% by weight of monovalent cation salts. Tolerance decreases as the valency of cations increases. Solutions are stable between pH 4 to 11; viscosity peaks between pH 6 to 8. Solutions are susceptible to bacterial, heat, enzyme and UV degradation.

Xanthan Gum

Description: Xanthan gum is an anionic polysaccharide derived from the fermentation of the plant bacteria X*anthomonas compestris*. It is soluble in hot or cold water and gives visually hazy, neutral pH solutions. Grades that provide high light transmittance are available. Xanthan gum will dissolve in hot glycerin.

Rheology: Xanthan gum solutions are typically in the 1500 to 2500 cps range at 1%; they are pseudoplastic and especially shear-thinning. In the presence of small amounts of salt, solutions show good viscosity stability at elevated temperatures. Solutions possess excellent yield value.

Compatibilities: Xanthan gum is more tolerant of electrolytes, acids and bases than most other organic gums. It can, nevertheless, be gelled or precipitated with certain polyvalent metal cations under specific circumstances. Solutions show very good viscosity stability over the pH 2 to 12 and good tolerance of water-miscible solvents (30 to 50% of solution weight). Xanthan gum is compatible with most nonionic and anionic gums, featuring useful synergism with galactomannans. It is more resistant to shear, heat, bacterial, enzyme and UV degradation than most gums.

Carrageenan

Description: Carrageenan is an anionic polysaccharide, extracted principally from the red seaweed *Chondrus crispus*. Carrageenan is available in sodium, potassium, magnesium, calcium and mixed cation forms. Three main structural types exist: Iota, Kappa, and Lambda, differing in solubility and rheology. The sodium form of all three types is soluble in both cold and hot water. Other cation forms of Kappa and Iota are soluble only hot water. All forms of Lambda are soluble in cold water. Carrageenan solutions are typically clear, and of alkaline pH.

Rheology: All solutions are pseudoplastic with some degree of yield value. Certain Ca-Iota solutions are thixotropic. Lambda is non-gelling. Kappa can produce brittle gels; Iota can produce elastic gels. All solutions show a reversible decrease in viscosity at elevated temperatures.

*Compatibilities: I*ota and lambda carrageenan have excellent electrolyte tolerance, kappa's being somewhat less. Electrolyte will, however, depress solution viscosity. Solutions show a fair to good tolerance of water-miscible solvents (10 to 30% of volatile solvents; up to 80% of glycerin). The best solution stability occurs between the pH 6 to 10. Carrageenan is compatible with most nonionic and anionic water-soluble thickeners. It is strongly synergistic with locust bean gum and strongly interactive with proteins. Solutions are susceptible to shear and heat degradation.

Gum Arabic (Acacia)

Description: Gum arabic is an anionic polysaccharide collected as the dried exudate from the acacia tree (*Acacia senegal*). Sold as the naturally occurring mixed Ca, Mg, and K salt, it is soluble in hot or cold water and gives clear solutions of neutral to acidic pH.

Rheology: Gum Arabic is a very low viscosity gum, with possible concentrations of up to 50% in water. Below a 40% concentration, solutions are Newtonian; above 40% they are pseudoplastic. Solutions show reversible viscosity loss at elevated temperatures and possess yield value at sufficient concentration.

Compatibilities: Gum arabic is compatible with moderate amounts of most salts, acids and alkalis, as well as with most water-soluble thickeners. Solutions are stable between pH 1 to 14; viscosity peaks at pH 6, dropping sharply below pH 5 and above pH 7. Electrolytes depress solution viscosity. Solutions are tolerant of water miscible solvents to about 50% of solution weight, and are susceptible to bacterial, heat and UV degradation.

Gum Tragacanth

Description: Gum tragacanth is an anionic polysaccharide collected as the dried exudate from shrubs of the genus *Astragalus*. It is composed of two major components: water-swellable bassorin and water-soluble tragacanthin. It produces hazy, surface active solutions of slightly acidic pH in hot or cold water. Its ability to lower surface tension and interfacial tension, in addition to thickening, makes gum tragacanth an effective emulsion stabilizer.

Rheology: Gum tragacanth is available in grades of varying quality and refinement with 1% viscosities of about 300 cps to 3000 cps. Solutions are pseudoplastic, show a reversible decrease in viscosity at elevated temperatures and possess good yield value.

Compatibilities: Gum tragacanth solutions are tolerant of monovalent and divalent cations, but are precipitated by trivalent species. They show a limited tolerance of water-miscible solvents, but provide synergistic viscosity with glycerin. Solutions are stable between pH 2 to 11, with some loss in viscosity at pH <5. Gum tragacanth is compatible with most water-soluble thickeners. Solutions are unusually resistant to bacterial growth and degradation.

Sodium Alginate

Description: Sodium alginate is an anionic polysaccharide extracted principally from the giant kelp *Macrocystis pyrifera* as alginic acid and neutralized to the sodium salt. It is soluble in hot or cold water and gives somewhat hazy solutions of neutral pH.

Rheology: Sodium alginate is available in grades ranging from about 20 cps to about 1000 cps at 1%. Solutions are pseudoplastic and show a reversible decrease in viscosity at elevated temperatures. Sodium alginate solutions lack yield value.

Compatibilities: Sodium alginate has limited compatibility with monovalent salts. Polyvalent cations tend to cause gelation or

precipitation. Solutions show a fair to good tolerance of water miscible solvents (10 to 30% of volatile solvents, 40 to 70% of glycols). Highly refined sodium alginate shows good stability over the pH 3 to 10. Sodium alginate is compatible with most water soluble thickeners and resins. Its solutions are more resistant to bacterial and enzymatic degradation than those of many other organic thickeners.

Sodium Carboxymethyl Cellulose

Description: Sodium carboxymethyl cellulose (CMC) is an anionic polymer made by swelling cellulose with NaOH and then reacting it with monochloroacetic acid. It is soluble in hot or cold water and gives neutral solutions. Solutions of refined grades are clear and colorless.

Rheology: CMC is available in grades ranging from 10 cps at 2% to 5000 cps at 1%. Most CMC solutions are slightly thixotropic; some strictly pseudoplastic grades are available. All solutions show a reversible decrease in viscosity at elevated temperatures. CMC solutions lack yield value.

Compatibilities: In general, stability with monovalent salts is very good; with divalent salts good to marginal; with trivalent and heavy metal salts poor, resulting in gelation or precipitation. CMC solutions offer good tolerance of water miscible solvents (30 to 50% of solution weight), good viscosity stability over the pH 4 to 10, compatibility with most water-soluble nonionic gums and synergism with hydroxyethyl cellulose and Hydroxypropyl cellulose. Solutions are susceptible to shear, heat, bacterial, enzyme, and UV degradation.

Methyl Cellulose, Hydroxypropylmethyl Cellulose

Description: Methyl cellulose (MC) and hydroxypropylmethyl cellulose (HPMC) are nonionic and anionic polymers respectively made by swelling cellulose with NaOH and then reacting it with methyl chloride alone (MC) or methyl chloride and propylene oxide (HPMC). Both are soluble in cold water and give clear, colorless and surface-active solutions of neutral pH.

Rheology: MC is available in grades from very low to high viscosity. HPMC is available in grades from very low to extremely high viscosity. Solutions are pseudoplastic and have characteristic gelation temperatures between 50°C and 85°C, depending upon the grade. These gels are reversible with return to fluidity on cooling. Below the gelation temperature, solutions show a decrease in viscosity as temperature increases. Non-gelled solutions lack yield value.

Compatibilities: MC and HPMC are compatible with most inorganic salts, limited only by the electrolyte concentration at which the polymers are salted out. HPMC will tolerate somewhat higher electrolyte concentrations than MC. Both polymers show good viscosity stability between the pH 3 to 11 and good tolerance of water-miscible solvents. Some grades are soluble in specific polar organic liquids. MC and HPMC are more resistant to bacterial and enzymatic degradation than most cellulosics.

Hydroxyethyl Cellulose

Description: Hydroxyethyl cellulose (HEC) is a nonionic polymer made by swelling cellulose with NaOH and reacting with ethylene oxide. HEC is soluble in hot or cold water and gives clear, colorless, neutral pH solutions.

Rheology: HEC is available in grades ranging from 2 cps to 80000 cps at 2%. Solutions are pseudoplastic and show a reversible decrease in viscosity at elevated temperatures. HEC solutions lack yield value.

Compatibilities: HEC solutions are compatible with most inorganic salts, limited only by the electrolyte concentration at which the polymer is salted out. Polyvalent inorganic salts will salt out HEC at lower concentrations than monovalent salts. HEC solutions show only a fair tolerance of water-miscible solvents (10 to 30% of solution weight), but good viscosity stability over the pH 2 to 12. They are compatible with most water-soluble gums and resins, and are synergistic with CMC and sodium alginate. HEC solutions are susceptible to bacterial and enzymatic degradation.

Hydroxypropyl Cellulose

Description: Hydroxypropyl cellulose (HPC) is a nonionic polymer made by swelling cellulose with NaOH and then reacting it with propylene oxide. HPC is soluble in cold water at <40°C and gives clear, colorless, surface-active solutions of pH 5 to 9.

Rheology: HPC is available in grades ranging from 10 cps to 5000 cps at 1%. Solutions are pseudoplastic and lack yield value. HPC will precipitate from water solutions above 45°C.

Compatibilities: HPC is compatible with most inorganic salts, limited only by the electrolyte concentration at which the polymer is salted out. Polyvalent inorganic salts will salt out HPC at lower concentrations than monovalent salts. HPC has better solubility in most polar liquids than in water. Aqueous solutions can tolerate unlimited dilution with most water-miscible solvents. The best viscosity stability is achieved in the pH 6 to 8. HPC is compatible with most water soluble gums and resins, and it is synergistic with CMC and sodium alginate. Solutions are susceptible to shear, heat, bacterial, enzyme and UV degradation.

Hydroxypropyl Guar Gum

Description: Hydroxypropyl guar (HPG) is a nonionic derivative of guar gum. HPG is made by reacting guar gum with propylene oxide. It is soluble in hot or cold water and gives clear solutions.

Rheology: HPG gives high viscosity, pseudoplastic solutions that show a reversible decrease in viscosity at elevated temperatures. HPG solutions lack yield value.

Compatibilities: HPG is compatible with high concentrations of most salts. It shows good tolerance of water-miscible solvents (up to about 60% by weight) and much better compatibility with minerals than does guar. HPG offers very good viscosity stability in the pH range 4 to 10 and is more resistant to bacterial and enzyme degradation over native guar and many other organic thickeners.

Honour/Awards

Prof. B.P. Chatterjee has joined as Emeritus Professor of West Bengal University of Technology, Salt, Lake Kolkata 700064 and Fellow of All India Council for Technical Education, New Delhi.

Prof. Ms. Anakshi Khare was awarded Scientist Emeritus fellowship of C.S.I.R., New Delhi on "Design and development of oligosaccharides synthesis related to bacterial cell wall through microwave irradiation" which she joined at Institute of Engineering and Technology, Lucknow.

Dr. P.L. Soni is bestowed with "21st Century Health Excellence Award" which was presented on 25th March, 2008 at India Habitat Center, New Delhi by Economic Growth Society of India. He has also received the Bhartiya Udyog Ratna award on 28th May, 2008 in Goa.

Prof. Tanmaya Pathak of I.I.T., Kharagpur, visited (June-July, 2008) Department of Molecular Pharmacochemistry, CNRS/Grenoble University, Meylan, France in connection with a collaborative project entitled "Synthesis and Biological Studies of Azido and Aminohexopyranosyl Nucleosides and Aminohexopyranose Containing Oligomers." The project is funded by the Indo French Centre for the Promotion of Advanced Research, New Delhi.

Prof. Rekha S. Singhal's (ICT, University of Mumbai) review paper entitled "Industrial production, processing, and utilization of sago palm-derived products**"** published in *Carbohydrate Polymers*, Volume 72, Issue 1, April 2008, Pages 1-20 by Singhal, R.S.; Kennedy, J.F.; Gopalakrishnan, S.M.; Kaczmarek, A.; Knill, C.J.; Akmar, P.F., had found 5th place in the top 25 most downloaded articles.

Prof. Ghanshyam S Chauhan of H.P. University, Shimla, is at present at Chemcial & Biological Engineering Department of Gyeongsang National Univeristy, Jinju, Republic of Korea (South Korea) as Brain Pool Fellow of the Korean Foundation of Science and Technology. He joined there on February 01, 2008. The fellowship is initially for one year and can be extended for another year.

Chemistry Department, Lucknow University, Lucknow in collaboration of Association of Carbohydrate Chemists & Technologists of India (ACCTI) has organized Prof. M.P. Khare memorial lecture series on Feb. 20, 2008. Following speakers from USA and India have delivered the Invited lectures-

S. No.	Speaker	Title
1	Prof. Xi Chen University of California, Davis One Shields Avenue Davis, CA 95616, USA	*Chemoenzymatic Approaches for Chemical Glycobiology*
2	Dr. R. Ravishankar Structure & Molecular Biology Division C.D.R.I Lucknow, India	*Novel structural weapons to fight M. tuberculosis*
3	Prof. Peng George Wang Department of Chemistry Ohio State University Columbus, OH, USA	*Glycopharmaceuticals: A spoon of sugar makes the medicine go down.*

ACCTI YOUNG SCIENTIST AWARDS, 2007

To encourage young students, the Association of Carbohydrate Chemists & Technologists (India) gives cash award of Rs. 1000.00 (Rupees one thousand only) and a citation for the best oral/poster presentation at the 'Carbohydrate Conference' every year. Only research scholars, research associates etc. (below the age of 30) are eligible for this award.

At the XXII Carbohydrate Conference, held during Dec. 13-15, 2007, at National Institute of Pharmaceutical Education & Research (NIPER), SAS Nagar (Mohali), Punjab, paper entitled; "Synthesis of Oligosaccharides Corresponding to Agarinan C isolated from Agaricus bisporus for Anticancer Studies" by Satish Malik and K.P. Ravindranathan Kartha was judged as the best oral presentation. The paper entitled "Study on the Sialoglycoconjugate Specific Antibodies in Non-Small-Cell Lung Carcinoma" by Sangeeta Mehta, S. C. Sharma, S. Radhika, D. Behera & S. Ghosh was judged the best poster presentation. We express our heartiest congratulation to Mr. Satish Malik and Dr. Sangeeta Mehta.

Satish Malik is presentely working as Ph.D scholar (SRF) in the Department of Medicinal Chemistry at the National Institute of Pharmaceutical Education and Research (NIPER), Mohali under the guidance of Prof. K.P. Ravindernathan Kartha, since July 2005. His thesis work is on "Synthesis of Oligosaccharides Corresponding to Agarinan C isolated from *Agaricus bisporus* for Anticancer Studies". He did his B.Sc. (Medical) with 1st class from DAV college, Ambala City in the year 2002 and M.Sc. (Organic Chemistry) with 1st class in the year 2004 from M.L.N. College Yamuna Nagar under Kurukshetra University. After that he worked as Research Chemist in Medicinal Chemistry Department at Ranbaxy NDDR division, Gurgaon until july 2005 and qualified June 2004 CSIR-UGC NET(JRF) in chemical sciences.

During free periods he loves to play cricket, football and chess.

Sangeeta Mehta has done Ph.D. on "Biological significance of disease specific glycoconjugate specific lectin in lung carcinoma" from Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India. She has presented/attended many national meetings /seminar including Indo-USSymposium on Stem Cell Identification andCharacterization, 2007. She is member of Association of Basic Medical Scientist (ABMS), India, life Member of Indian Association Cancer Research (IACR), India and life member of Indian Society for Study of Lung Cancer (ISSLC), India

MS. LUCID COLLOIDS LIMITED AWARD- 2007

To encourage research on hydrocolloids, Ms. Lucid Colloids Limited, Mumbai, offers a cash award of Rs. 5000.00 (Rupees five thousand only) and a citation for the best paper presentation on hydrocolloids since 2003. At the XXII Carbohydrate Conference, held during Dec. 13-15, 2007 at National Institute of Pharmaceutical Education & Research (NIPER), SAS Nagar (Mohali), Punjab, the paper entitled "Oxidized Guar Gum-Based Hydrogels as Stimuli Sensitive Carrier for Insulin Delivery" by Ghanshyam S. Chauhan and **Kalpana Chauhan** was selected for the award. We express our heartiest congratulation to Ms. Kalpana Chauhan

Kalpana Chauhan has submitted recently her Ph.D (Polymer Chemistry) in the Faculty of Physical Sciences, Himachal Pradesh University, Shimla on "Modification of Starch and Guar Gum to Respective Polycarboxylates for use in Water Technology and Drug Delivery" under the supervision of Dr. Ghanshyam S. Chauhan. Till recently she was project fellow in a major research project "Development of Novel Green Flocculants for the Treatment of Industrial Effluents" sponsored by the University Grants Commission, New Delhi.

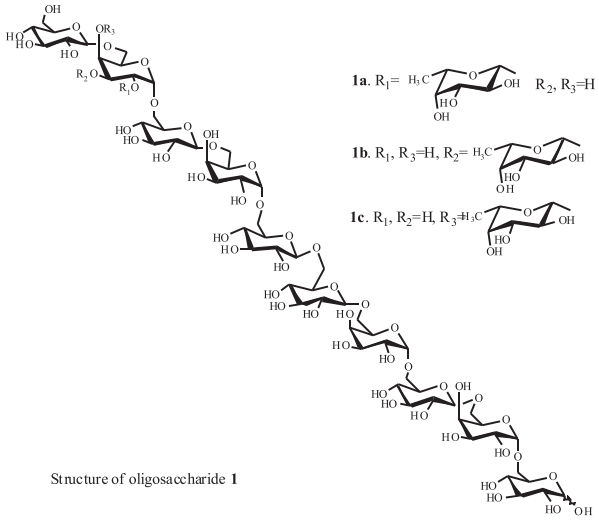
She obtained B.Sc. (Med.), M.Sc (Organic Chemistry) and M.Phil. (Polymer Chemistry) degrees in the year 2000, 2002 and 2003, respectively with first class from the Himachal Pradesh University. Apart from the constant and excellent academic record through out the carrier she have a keen interest in nature, bird watching and gardening.

FOLLOWING ARE THE ABSTRACTS OF YOUNG SCIENTIST AWARDEES PRESENTED AT CARBO XXII-

Synthesis of Oligosaccharides Corresponding to Agarinan C isolated from *Agaricus bisporus* for Anticancer Studies Satish Malik and K.P. Ravindranathan Kartha

Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research, Sector-67, S. A. S. Nagar-160 062, Punjab, India

Intensive exploratory work on *Agaricus bisporus, leader of mushroom* has led to the unraveling of an "active" polysaccharide, 'Agarinan C', composed of glucose, galactose and fucose in the ratio of 1.5:1:0.25. Agarinan C has shown equal or better activity than the marketed antitumor polysaccharide drugs lentinan and krestin. Since the oligosaccharide isolation from mushroom is very low yielding and to facilitate further work toward the elucidation of their structural/conformational properties as well as biological activity, we have decided to synthesize the oligosaccharide repeating unit **1**. The major difficulty associated with the chemical synthesis of this **oligosaccharides** is the necessity to introduce four 1,2-cis linkages stereoselectively. The methods and strategy developed for the synthesis of its intermediate oligosaccharides will be discussed in the talk.



Structure of oligosaccharide **1**

Study on the Sialoglycoconjugate specific antibodies in Non-Small-Cell Lung Carcinoma

[1]Sangeeta Mehta, [1]SC Sharma, [2]S Radhika, [3]D Behera AND [4]S Ghosh

[1]Dept. of Radiotherapy, [2]Dept. of Cytology and Gynaec Pathology, [3]Dept. of Pulmonary Medicine, [4]Dept. of Experimental Medicine and Biotechnology P.G. Institute of Medical Education and Research, CHANDIGARH-160012

Notable changes occur in the carbohydrate architecture of the cells during the process of tumour formation. These changes can be detected by the immune system and an immune response can be mounted against such changes. The antibodies against modified carbohydrate antigens can be detected in the serum of patients having cancers. The presence of carbohydrate specific antibodies has been reported in various cancers including leukemia. But there is no report regarding the status of antibodies in the bronchial environment in the lung cancer patients. Therefore, this study was undertaken to analyze the antibodies in bronchoalveolar lavage fluid (BALF) of non-small-cell lung cancer (NSCLC) patients and also to determine if these antibodies could identify any molecule on the tumour cells. We observed that the BALF of NSCLC patients contained very high amounts of IgG against the sialoglycoconjugates (fetuin and ganglioside GM3) as compared to controls. Furthermore, the level of fetuin specific IgG was higher than that of asiofetuin specific IgG; and also the level of GM3 specific IgG was higher than GM3 specific IgM. The IgG could specifically interact with a membrane glycoprotein on the NSCLC cells. This is the first report regarding the presence of sialoglycoconjugate specific IgG in the BALF of NSCLC patients. It is possible to design a simple ELISA based assay for detection of IgG in BALF of NSCLC patients for the early diagnosis of the patients.

Oxidized Guar Gum-Based Hydrogels as Stimuli Sensitive Carrier for Insulin Delivery

Ghanshyam S. Chauhan*, Kalpana Chauhan

Department of Chemistry, Himachal Pradesh University, Shimla 171005

In resent years the development of stimuli sensitive release polymeric systems for the site specific release of the bioactive molecules has been a subject of significant pharmaceutical importance. The advantages of material to be used in such applications should be cover biocompatibility, cost-effectiveness and easy availability. The approach for targeted drug delivery include the reduction of required resources for therapy, an increase of the drug therapeutic index and the prevention of frequent, unpleasant or expensive treatments. Thus polysaccharides make natural choice of materials. In the present study, the objective was to achieve the carrier mediated colon intended drug delivery utilizing guar gum based hydrogels. In view of the above, an attempt to modify guar gum as alternative material for the use in intended drug delivery has been attempted. It was modified by a polyelectrolyte and the present paper discusses its preparation and characterization of such stimuli sensitive polyelectrolyte by solvent free oxidation using *in situ* generated nitrogen oxides as oxidizing agents at the ambient temperature. He resultant functionalized guar gum containing carboxylic acid was characterized by calcium acetate method, FTIR, ^{13}C NMR, elemental analysis (C and H) and swelling responsiveness in simulated gastric fluid (pH 1.2) and simulated intestinal fluid (pH 7.4). It was used to study the release of insulin a model drug. The insulin release was observed to be polymer structure dependent.

Organizing Secretary's Report on CARBO-XXII

The conference was held at the National Institute of Pharmaceutical Education & Research (NIPER), SAS Nagar during December 13-15, 2007. Organized by the Department of Medicinal Chemistry and attended by about 175 participants & delegates, the three days' proceedings were conducted at the NIPER Convention Centre in the midst of NIPER Campus. **Considering the importance of carbohydrates in processes such as cell recognition, cell growth & defense, binding of bacterial/viral antigens or bacterial toxins to mammalian cells, inflammatory responses, cancer metastasis, etc, in addition to that in food and nutrition, that has led to growing activities in the pharmaceutical industries world wide for the development of carbohydrate-based drugs/ therapeutics and hence its great relevance to the educational and research activities of NIPER, the theme of CARBO-XXII was kept as, "**Carbohydrates: Chemistry, Biology & Industrial Applications**".**

At the inaugural session attended by about 325 delegates Professor P. Rama Rao, Director NIPER addressed the gathering welcoming one and all to the Institute and to its Campus. Subsequently Dr. P.L. Soni gave his Presidential remarks followed by the introduction of the Department of Medicinal Chemistry, NIPER by Professor A.K. Chakraborti, Head of the Department. Professor Rob A. Field, John Innes Centre, Norwich, UK then did the ceremonial lamp-lighting and presented his inaugural address on, "The biofuels agenda: Opportunities and challenges for carbohydrate chemistry and biochemistry". Dr. A.K. Sen then gave his Secretarial remarks and Professor K.P.R. Kartha, organizing Secretary, introduced the programme of the three days' conference. The Life Time Achievement Award ceremony was then held in which the award was presented to Sri N.C. Dhuldhoya, Lucid Colloids Ltd., Mumbai for his valuable contribution to the Indian gum industry in particular and to the Indian carbohydrate community & ACCT(I) in general. The inaugural function was concluded by the vote of thanks offered by Professor K.K. Bhutani, Dean, NIPER.

There were nine technical sessions held over three days covering four plenary lectures, sixteen invited lectures and eighteen oral presentations besides five poster sessions; and various aspects of carbohydrate chemistry as in progress in the laboratories of the presenters were brought to light and were deliberated during those sessions. The subjects that found coverage during the Meeting include synthesis, modification & application, hydrocolloids and glycobiology. The technical sessions were started with a plenary lecture by Dr. R.A. Vishwakarma, Nicholas Piramal Research Centre, Mumbai on the chemical biology of glycosylphosphatidylinositol molecules. The technical session on glycobiology on the second day of the conference was held in honor of Professor B.P. Chatterjee on account of his superannuation acknowledging his long-standing services to the Association and to the community. Professor Chatterjee spoke eloquently on, "Reminiscence: Carbohydrate, Lectin, glycobiology….. A path to follow disease markers". That session was also marked by a scholarly address given by Dr. Harry J. Jennings, National Research Council Canada on polysialic acid vaccines against bacterial meningitis and cancer. Harry is one of the top most authorities in the world on the subject. Other speakers from outside the country included Professor H. Ishida, Gifu University, Japan who spoke on novel methods of constructing glycolipids and glycopeptides in the laboratory and Professor Ulf J. Nilsson, Lund University, Sweden on the development of high affinity galectin inhibitors. The last plenary lecture on day three was delivered by Professor V.S. Parmar, University of Delhi on the chemical synthesis of modified carbohydrates and nucleosides with stress laid on "greener" methods of synthesis. Presenters of the invited lectures include Dr. N.G. Ramesh, IIT, Delhi, Professor U.C. Banerjee, NIPER, Dr. V. Kumar & Dr. P.K. Gupta, FRI, Dehra Dun, Dr. S.N. Moorthy, CTCRI, Trivandrum, Dr. H. Das, IGIB, Delhi, Dr. S. Ghosh, PGIMER, Chandigarh, Professor D. Loganathan, IIT, Madras, Dr. R.P. Tripathi, CDRI, Lucknow, Professor G.S. Chauhan, HPU, Shimla, Dr. V. Singh, CFTRI, Mysore, Dr. V.K. Varshney, FRI, Dehra Dun, Professor N.K. Khare, LU, Lucknow and Dr. A.K. Prasad, DU, Delhi.

The General Body Meeting of the Association was held in the evening on day one of the Conference and the Minutes of the Meeting will be reported by the Hon. Secretary of the Association. It was decided that CARBO-XXIII will be held in Bhavnagar with Professor H.C. Trivedi, Vice-Chancellor, Bhavnagar University as the Organizing Secretary.

KPR Kartha, Organizing Secretary.

Welcome new members of ACCTI (2007)

All old and new members are requested to send their current complete address, telephone no., e mail address etc to the Editor, CNL (CNL.ACCTI@gmail.com) to make the list more meaningful. Please also motivate your colleague, friends and students to become member of the ACCTI to strengthen the Association. Thanks.

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Men have a better time than women; for one thing, they marry later; for another thing, they die earlier.

- H.L. Mencken

I don't worry about terrorism, I was married for two years.

- Sam Kinison

Trends in Carbohydrate Research (TCR)

It gives me immense pleasure to inform that Association of Carbohydrate Chemists & Technologists India is launching Trends in Carbohydrate Research (TCR) in December 2008, which will be an international scientific journal devoted for promotion and utilization of latest research and developments related to various scientific and technological aspects of carbohydrates.

The ACCTI (www.geocities.com/acctindia) was founded in 1986 to provide a common platform for people from carbohydrate related industry on one hand and scientists and technologists working in the field of carbohydrate chemistry in academic and research institutes on the other hand, to exchange ideas, developments and industrial requirements related to carbohydrates. The ACCTI, in collaboration with R&D institutes and Universities, provide a productive platform through annual conferences to a wide array of the researchers, technocrats, academicians, industrialists and planners . As a commitment to encourage research, education and communication, the ACCTI also publishes the research work presented in the conference in form of a book titled "Trends in Carbohydrate Chemistry". Nine volumes of the book have been published so far. The electronic form of all these volumes will also be available on the journal's website.

The year 2007 witnessed the successful hosting of XXII CARBO Conference, at National Institute of Pharmaceutical Education and Research (NIPER), Chandigarh and XXIII Carbo is going to be held at Bhavnagar University, Gujrat, on 3-5 December, 2008. This is a matter of pride and pleasure that the ACCTI in collaboration with International Carbohydrate Organization, is also going to host the first international conference in 2014 at Indian Institute of Science, Bangalore.

The TCR will be a subscribed and peer-reviewed journal and will be published quarterly. The website www.trendscarbo.com to be launched shortly may be surfed for hands on experience.

Aims and Scope

The overall aim of the TCR is to advance and disseminate knowledge in all related areas of carbohydrates to benefit the whole carbohydrate's community. It offers an international forum for exchange of latest research and developments related to various scientific and technological aspects of carbohydrates and publishes original research in form of normal length research papers, short reports, review articles in the following facets lie well within the scope of this journal.

1. Carbohydrate polymers having current or potential industrial applications, their structures, properties, and modifications both chemical and microbiological.

2. Chemistry and biology of carbohydrates including synthesis, structure elucidations, stereochemistry, reaction mechanisms, isolation of natural molecules, physicochemical studies, biosynthesis, metabolism, degradation, structural and functional biochemistry, enzymes- their action and mechanisms, immunochemistry, and glycobiology.

3. Analytical methods / chemistry of carbohydrate

4. Technologies for conversion or production of industrially important carbohydrates including methods, processes, and systems.

The journal will also publish reports of conferences, book reviews, news items, details of forthcoming meetings and contributions describing industrial applications.

Audience will include Scientists, Researchers, Technologists, Academia, Industrialists, R&D institutes, Universities, Planners, Users and Producers of carbohydrate products.

GUIDELINES FOR AUTHORS For TCR

Contributors are advised to submit their manuscript as electronic files, by e-mail to Dr. P.L.Soni, Editor in Chief E-mail: <soniplin@yahoo.co.in> or <sonitcr@gmail.com> . The preferred software for text is MS Word for Windows version 6.0 onwards or upwards. Illustrations may be provided in Corel Draw, ISIS Draw, Chem Draw or any compatible format software or as picture in MS Word Version 6 onwards.

Manuscripts should be divided into: Title, Authors, Affiliations, Abstract, Introduction, Results and Discussion, Materials and Methods, Experimental Section, Conclusion, Acknowledgements, References, Tables, Figures, Schemes, Captions and Graphical Abstract for table of contents. All text must be double spaced throughout and pages numbered. Abbreviations should be defined the first time they are used, and a list of all abbreviations used should be provided. Suggestions for reviewers are welcome. The corresponding author's full mailing address, FAX numbers, and E-mail address if available, may be provided for speedy communications. **While entering the data following points with respect to text, references, and tables should be taken care of:**

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EXECUTIVE COMMITTEE MEMBERS (2007-2008)

The new executive committee members for the years 2007 & 2008 were elected by the General Body in the GB meeting of the ACCT(I) held on 26th November, 2006 at the XXIst Carbohydrate Symposium (Delhi University).

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Application along with subscription only by D.D. or M.O., in favour of **'Association of Carbohydrate Chemists & Technologists (India)' payable at Dehradun**, to be sent to the Hon. Treasurer, Dr. P. K. Gupta, Chemistry Division, Forest Research Institute, P.O. New Forest, DEHRA DUN, Uttaranchal, Pin - 248 006

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