MICROCRYSTALLINE CELLULOSE FROM CORNCOB, BAGASSE AND NEWSPRINT AND ITS UTILITY IN SOLID DOSAGE FORMS

Thesis
submitted in partial fulfilment of the
requirements for the degree of
DOCTOR OF PHILOSOPHY

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1983

THOUGHT FOR THE THESIS

Those who love hard work and love it all the better,
because, it is hard,

Those who try and fail and keep on trying,

Those who can suffer the loss of months of hard labour
and start all over again,

Those who cannot be discouraged,no matter what happens,

Are invited to undertake research.

Prof. E. Emmet Reid
Invitation to Chemical Research
1961.

BIRLA INSTITUTE OF TECHNOLOGY AND SCIENCE

PILANI RAJASTHAN

PHARMACY DISCIPLINE

CERTIFICATE

This is to certify that the thesis entitled "Microcrystalline Cellulose from Corncob, Bagasse and Newsprint, and its Utility in Solid Dosage Forms", submitted by B.G.Nagavi, ID No- 80PH 24007, in partial fulfilment of the requirements of Ph.D degree of the Institute, embodies original work done by him under my supervision.

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ACKNOWLEDGEMENT

A research scholor can never fully acknowledge the debts he owes to others. Inadequate as it may be, I do wish to express my gratitude to all those without whose association the present thesis would not have seen the light of the day.

I am indebted to Prof. B.M.Mithal, Professor of Pharmacy and Dean,Students Welfare Division, B.I.T.S. Pilani, for guiding the present work. I am grateful to Dr. C.R.Mitra, Director, B.I.T.S., Pilani, Prof. C.K.Atal, Director, R.R.L., Jammu, and Prof. S.S.Mathur, Group Leader, Pharmacy Discipline, B.I.T.S., Pilani, for the help rendered in the course of the present work.

Acknowledgement is made to FMC, USA, for sending free samples of MCC (Avicels) for the present study.

I am grateful to Dr.J.S.Chawla, Chairman, Cellulose Pulp and Board Division, R.R.L., Jammu, for facilities and constructive discussions. I am indebted to Dr.K.S.M.Sastry, Chairman, Mycology and Plantpathology Division, R.R.L., Jammu and remember with reverence Mrs.Sastry and the grand-mother for their natural affection and hospitality.

I thank my colleagues, Dr.Bhise, S.B., Dr. Bindal,M.C., Mr. Madamwar, D.B., Dr. Manavalan,R., Dr.Rao,M.N.A. and Mr. Shewade,D.G., for their generous aid and encouragement during the course of the work.

I hardly know how to express my deep sense of gratitude to my uncle, Prof. D.P. Nagavi, Professor of Mathematics, K.C.P. Science College, Bijapur, Karnataka, without whom, I would not have got the stint of Science, let alone the profession of Pharmacy. A special acknowledgement is recorded to my parents and wife, who have noding acquaintance of the present thesis. They have always been so patient, cooperative, supportive and understanding of the inordinate percentage of time I have devoted to the present work.

Last, but not the least my sincere thanks to Shri J.L.Kaul, Industrial Survey Division, R.R.L., Jammu, for expeditious typing of the manuscript.

Bali

(B. G. Nagavi)

Jammu
Date: 13|8|83.

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CHAPTER - I

INTRODUCTION

1.1 Cellulose a Versatile Natural Polymer

Man and cellulose have coexisted on this planet from times immemorial. Cellulose has formed the basis of good life through its conversion to many items of utility and luxury for the mankind; clothing, furniture, raw films, fuel and paper are some of the examples that immediately spring to ones mind. Of late, cellulose has been replaced by man-made polymers. However, it is hard to imagine life without cellulose. Billions of tons of cellulose is created every year by plants by photosynthesis.

Cellulose, the prime structural element of cellwalls of trees, higher plants, mosses, ferns, algae and fungi, owes its name to the French agriculturist A. Poyen (Hamilton and Mitchell, 1964). It is generally found in association with lignin, hemicelluloses etc. in varying proportions. Cellulose, is a complex and unique polysaccharide consisting of 1000 or more (depending on the source) anhydro-glucose units, joined by beta 1,4-glucosidic linkages (Haworth, et al, 1927) twisted at an angle of 180° around the chain axis at the linkage (Fig. 1). Starch a close relative of cellulose has alpha 1,4 and 1,6-glucosidic linkages of anhydroglucose units. The structure of cellulose illustrates a complex interwoven matrix with alternative haphazard (amorphous region) and sequential (crystalline region)

Fig. 1 : STRUCTURE OF CELLULOSE

The cellulose molecular chain — β-1 4 glycosidic linkages between anhydro glucose units

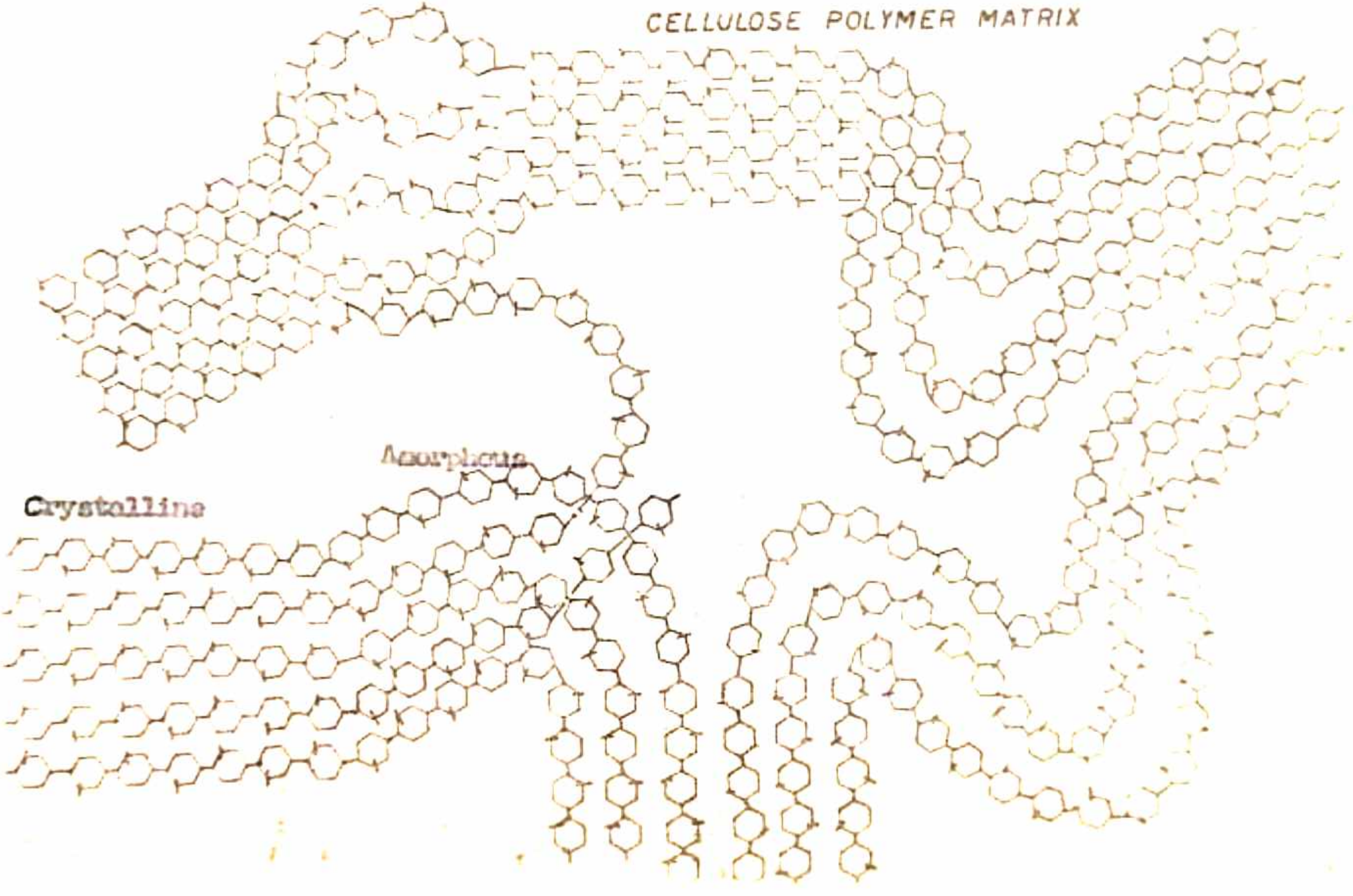
Fig. 1 STRUCTURE OF CELLULOSE

arrangement of the basic units (Fig.2). The thread like fibrils of cellulose are akin to match-sticks joined side ways, where each of them is stabilized by hydrogen bonding between - OH groups of adjacent molecules. Hence it forms a highly extended and hydrogen bonded conformation capable of further bonding into a sheet like organizations of chains. Inspite of the presence of numerous hydroxyl functions in the molecule, cellulose is insoluble in water and other organic solvents, polar as well as non-polar.

Cellulose is a versatile molecule that can undergo oxidation, substitution, hydrolysis, depolymerization etc. to give several compounds and its derivatives which are of prime importance in several fields of human endeavour. Some mile-stones in cellulose research are:

1838	A. Poyen coined the term cellulose
1875	Girard coined the term hydrocellulose
1928	Mayer and Mark postulated the crystalline nature of cellulose.
1937	Staudinger and Sorkin described the dual reaction rates of acid attack.
1941	Nickerson and coworkers spearheaded the use of acid-ferric chloride to study structure.
1943	Davidson demonstrated the levelling-off of molecular weight after initial acid hydrolysis.
1947	Battista and Coppick showed that level-off was a reflection of crystalline to amorphous ratio, fixed by past history of cellulose.
1956	Battista and coworkers prepared MCC from woodpulp & cotton.

Fig. 2: Arrangement of Basic Units in Cellulose



Terms commonly used in reference to cellulose are explained below:

1.	Cellulose:	A polymer of glucose in which several glucose units are linked by beta 1,4 bridge.
2.	Alpha cellulose	Cellulose whose average degree of polymerization (DP) is above 200 and it is insoluble in 17.5% NaOH.
3.	Beta cellulose	Cellulose whose average DP is between 10 and 200 but it is soluble in 17.5% NaOH.
4.	Gamma cellulose	Cellulose whose DP is about 10 and which is soluble in 17.5% NaOH.
5.	Cellulose I, Cellulose II and Cellulose III	I, II and III are the designations used to characterise the physical structure of the unit cell of the cellulose configuration. They vary in their cell dimensions (given elsewhere in the thesis).
6.	Bacterial cellulose	Pure cellulose produced by a bacterial agent such as *acetabacter xylinum*.
7.	Regenerated cellulose:	Cellulose precipitated out of a solution
8.	Oxy cellulose	It is the product obtained from cellulose by any oxidising procedure whereby carbonyl and/or carboxyl groups are introduced into the cellulose molecule.
9.	Hemi-cellulose	Includes lignin and non-cellulosic polysaccharides. Sum of beta and gamma cellulose which together constitute the principal non-

		cellulosic polysaccharide present in the holocellulose.
10.	Holo cellulose	All carbohydrate portion of cellulosic raw materials or Cross and Bevan Cellulose prepared by alternative chlorinations and hot sodium sulfite extractions to remove lignin. It includes cellulose and hemicellulose.
11.	Hydro cellulose	Acid depolymerised cellulose.
12.	Microcrystal:	Consists of a cluster of many long chain molecules held together laterally by non-covalent bonds. Polymer molecules are crystallised in the folder state, the extended linear state (fibrous) or gradations there of depending on the genetics of the polymer precursor.
13.	Fibrous Microcrystal	Small crystal aggregates attached side to side like matchsticks.
14.	Lamellar Microcrystals	Molecules folded on themselves into lamellar like structures.

1.2 Ultra-Structure of Cellulose

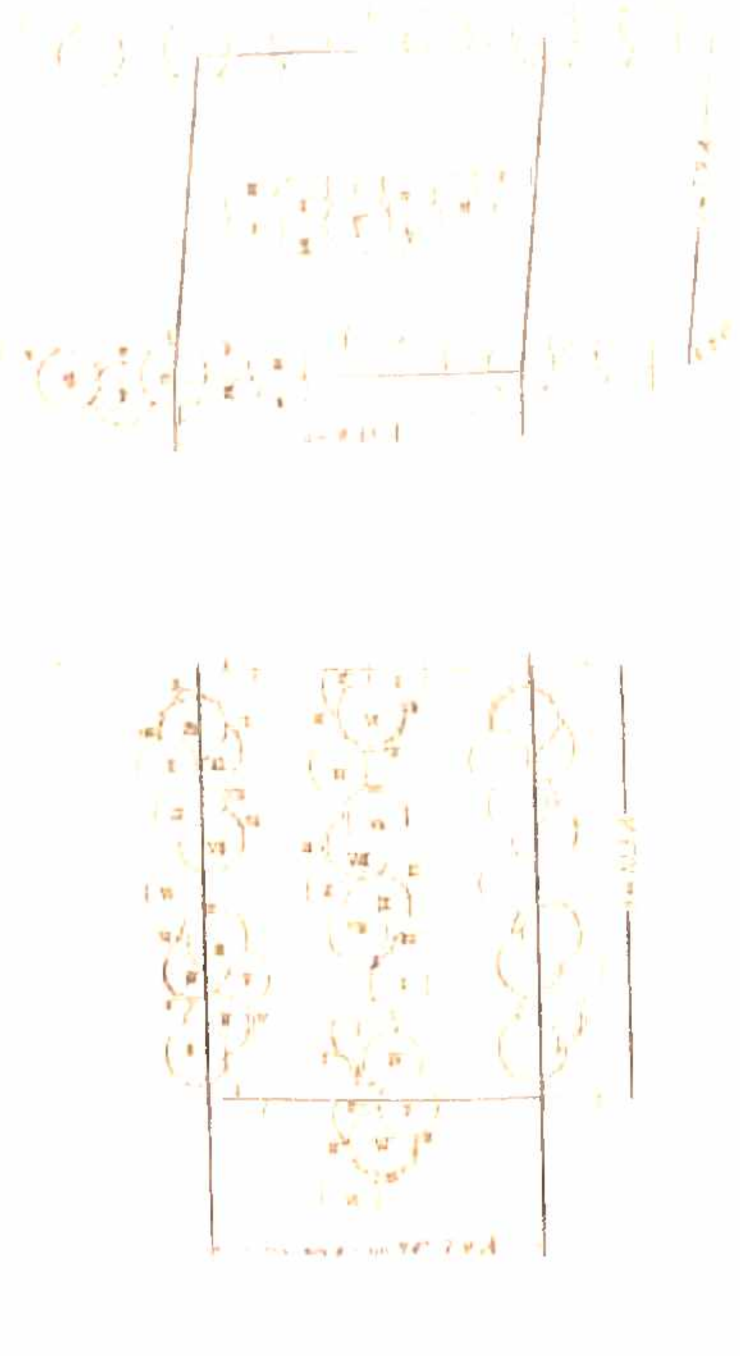
The three dimensional picture of cellulose is given below with a view to present, the status of the ultra-structure of cellulose as it stands today. Certain controversial points, relevant to the present thesis are emphasised. Ambiguities in the present cellulose structure models are highlighted.

Muhlethaler (1965) with the aid of negative staining showed that cellulose consisted of fibrillar and narrower structures called 'elementary fibrils'. These, are also referred to as 'micellar strands ' by the other authors. Elementary fibrils (EF) having a diameter of 35 A°, show a tendency to aggregate and form multiplets and finally a broad ribbon wound in the form of a tight helix (Fig.3). The molecules form flat ribbons by folding back and forth concertina fashion with the molecular chain tilted at some preferred angle to the ribbon axis. With the ribbon wound as a helix the molecular chain, axis becomes parallel to the fibril axis. Two glucose units are observed to be present in the folded region. The following unit cell dimensions have been proposed (Mayer - Misch, 1937) based on X-ray diffraction and other studies on cellulose

a = 8.35 A°, b = 10.3 A°, c = 7.9 A° and β = 84°

(see Fig. 3). Elementary fibrils consist of a crystalline core flattened parallel to the (101) plane. This crystalline core seems to be embedded in a cortex of para crystalline cellulose (10$\bar{1}$) . An insufficient order of the chain molecules in this cortex may be caused by the escaping water released during polymerization of glucose and crystallization of chain molecules. (Frey- Wyssling, 1954). The same author in the above reference states that amorphous and paracrystalline regions are same. But at a later stage elsewhere (Frey-Wyssling, 1969) the same author

Fig. 3 HELICAL / 3D ARRANGEMENT OF [illegible] [illegible] [illegible]



has mentioned that elementary fibrils are highly crystalline without a paracrystalline mantle.

According to Statton (1967), microfibrils (aggregated elementary fibrils) do not contain amorphous regions at least as a separate phase. Each microfibril is really a quasi single crystal and differences in X-ray diffractograms of different celluloses are due to lattice imperfections and not due to amorphous and crystalline regions in cellulose.

Mugli (1968) observed that no folds occur in cellulose chains. This observation contradicts earlier observation made by Muhlethaler. Cellulose is considered as a polycrystalline structure (Nickerbson,1950) traversing through crystalline and amorphous areas, matching with the first observation of (Frey- Wyssling, 1954). The amorphous region as visualised by Nickerbson may not be completely discorded, but may be bundles of nearly parallel chains not well enough oriented to give sharp interference spots. The authors opinion favours amorphous and crystalline chain formation in cellulose without clearly differentiating between them.

But, accessibility measurements on amorphous and crystalline oligo-saccharides suggest that the accessibility may be related to the perfection of the crystal lattice and does not measure the crystalline- amorphous ratio as previously supposed (Wadehra & John Manley, 1966). The accessibility of various celluloses remained constant during prolonged heterogonous hydrolysis, as observed by Wadehra and John Manley. This is at variance with the fringed micellar concept of the fine structure of cellulose, on the basis of which a substantial decrease on accessibility would be expected during hydrolysis.

As of today, crystalline and amorphous nature of cellulose is not clear and needs further investigations, since observations made in the past are contradictory. At this stage it may be safe to mention that cellulose has partly ordered and partly disordered regions without labelling them as crystalline and amorphous regions respectively. X-ray diffraction, Infrared studies and accessibility measurements vouch for ordered and disordered regions in cellulose. If it is accepted that cellulose has not crystalline and amorphous regions, the term Microcrystalline cellulose needs to be re-examined. A separate sub chapter under the title 'MCC or MFC (Micro Fine Cellulose/ Micro Fibrillated Cellulose) is included in the thesis giving experimental observations and possible interpretations.

The presence of elementary fibrils, microfibrils and fibres in cellulose is well documented and accepted. The presence of different regions, perfect and imperfect is also felt, as the ratio of the two has marked effect on strength, flexibility, reactivity and moisture content of cellulose. Presumably, due to biological necessity, cellulose has builtin imperfections like ordered and disordered regions. Lignin, a sealing wax in plants, found in the disordered region of cellulose, gives the plant necessary strength and rigidity with some amount of flexibility and softness.

1.3 Microcrystalline Cellulose

When ordinary cellulose (5%) was placed in water it settled down rapidly. When it was treated in a Waring blender for 15 mins. a stable colloidal dispersion was formed. The gel was opaque, snow white and had smooth fat like spreading properties (Battista, 1962). This simple process has been developed into a new technique to give commercially important commodity known as Microcrystalline cellulose (MCC), marked under the trade name Avicel by FMC Corporation, USA. Cellulose on hydrolysis with dilute mineral acids and mechanical disintegration gives microfibrils (MCC) with unusual physico-chemical properties.

MCC is defined as mechanically disintegrated level off Degree of Polymerization (LODP) cellulose. It can be prepared from all forms of celluloses, natural alkali, regenerated and degenerated. Raw material used for the preparation of Avicel is a special gradehigh alpha cellulose. LODP or DP cellulose is generally prepared by [illegible] purified cellulose in 2.5 N [illegible] for 15 [illegible] $\overline{DP}$ varies 200-250 for purified cotton to 15-30 for rayon tire cord.

TABLE-1

Level- off Basic m2 $\overline{DP}$ of Natural and Regenerated Fibres

Form of Cellulose	$\overline{DP}$	Reference
1. Natural fibres		Battista et al,1956
Ramie hemp	300-350	
Cotton purified	200-250	
2. Unbleached sulfite wood pulps	250-400	
3. Bleached sulfite wood pulps	200-280	
4. Bleached sulfite wood pulps	140-190	
5. Mercerized cellulose (18% NaOH,20°, 2 hrs)	70-90	
6. Vibratory milled wood cellulose	80-100	
7. Regenerated fibres		
Fortisan	40-60	
Textile yarns	30-50	
Tire yarns	15-30	

If the hydrolysis of pure cellulose is carried to completion, the product would be mainly glucose, with true limiting $\overline{DP}$ of one (Battista et al 1956). In practice, however, this is not true due to the presence of highly organized (crystalline) portion in the molecule which offers resistence to hydrolysis. It is only disorganized region which is prone to acid attack and subsequent hydrolysis. Once the disorganized region is knocked off, it attains level- off. Extent of pre-swelling of cellulose by alkali, severity of hydrolysis, extent of disintegration are some of the factors that affect the final $\overline{DP}$. Mild hydrolysis for example, favours the formation of longer, less acid soluble crystalline chains. In contrast, drastic hydrolysis promotes the formation of very short, more acid soluble crystalline material. In both cases, 1,4-glucosidic linkage is broken to give lower $\overline{DP}$ molecules. Microfibrils so formed on mechanical disintegration give a fibrous free slurry which on drying yields a fine, free flowing MCC. It is observed that the degree of depolymerisation, method of disintegration and drying play an important role in developing the inner structure of MCC. MCC microfibrils (Microcrystals) are individually distinct particles isolated from cellulose matrix. So far microfibrils (microcrystals) of celluloses, amyloses, collagens, nylons and polyesters have been reported (Battista, 1975). As such MCC is not a chemical but physical derivative of cellulose which is very fine and free flowing.

1.4 Applications of MCC

MCC finds wide application in pharmaceutical and other industries. In tablet formulations MCC is used as an inert diluent, disintegrant and lubricant. Due to high bonding nature of MCC, granulation before punching of the tablets is not required. Simple weighing, mixing and compression gives tablets of required qualities. MCC with slightly larger particle size may be used to improve flow of fine and very fine powders, while MCC with lower particle size may be used for the direct compression of coarser, granular or crystalline materials (Avicel Bulletin pH-6). Since avicel shows fast wicking rate for water compared to starch and lactose, tablets disintegrate in a few seconds (Avicel Bulletin pH-10). MCC is a non reactive organic material with very low levels of organic and inorganic contaminants. This makes it compatible with almost all types of drugs and other additives in dosage forms. MCC range in the formulations varies between 10-50 % depending on the type of dosage form.

Some applications of MCC have been tabulated in table 2.

TABLE- 2

Some Applications of MCC

Application	Role of MCC	References
Tablets	inert binder, diluent, disintegrant, lubricant, sugar coating additive	Walking and Shangraw, 1968 Sixsmith,1977
Suspensions	Suspending agent, stabilizer thickening agent	Parera.E,1977; Marshessault et al, 1961
Emulsions	Emulsifier, stabilizer	Parera,E, 1977
Chromatography	TLC, column and ion exchange chromatography	Wolfrom et al, 1965; Wolfrom, Busch et al.1965
Derivatives	Controlled particle size of MCC	-
Ceramics	Plasticity, rapid prefired glaze hardening	Bondi, 1965
Food	Non nutritive filler, reduces calorific value	Battista,1964
Cosmetics	Retains volatile principles	Fox et al,1963
Paints	Flow control, brush control and viscosity control	Avicel Bulletin Paints

Other applications of MCC not listed above are:

1) To control heat shock in frozen desserts
2) In canned convenience foods (meat, fish and poultry) containing stable heat sterilized salad dressings.
3) MCC is a precursor of unique structural products from which spheres or massive carbon or graphite structures may be made.

MCC is used in combination with CMC (12-16%) to produce stable suspensions/gels that have pharmaceutical and other applications. Characteristics of MCC-CMC used as food grade are given in table 3.

TABLE-3

Properties of MCC- CMC, Food Grade

Properties	Grade 581	Grade 501	Ref.
Composition			
MCC	89	91.5	Battista(1975)
CMC	11±1	8.5±1	
Physical form	White,water dispersible powder		
Particle size(average) microns	35	35	
Moisture, %	5	5	
Bulk density	31	31	
Ash %	2	2	
Heavy metals, ppm	10	10	
Iron, ppm	5	5	
pH, 1-2%	6-8	6-8	
Viscosity,cp	120±40 (1.2% conc.)	120±40 (2.1% conc)	

1.5 Cellulosic Wastes

A huge amount of cellulose goes waste either in intermediate or terminal stages of utilization or processing. Further more, many of the end-products of such efforts are themselves short lived and enter the garbage heaps. Different types of cellulosic wastes include (Reese, 1972):

Agricultural wastes – leaves, stalks, rice and other hulls, bagasse etc.

Food processing wastes – fruit peels, pulp, vegetable trimmings

Wood wastes – chips, bark, saw dust, paper mill fines

Municipal wastes – 40–60% of solid wastes, chiefly as garbage and waste paper.

In India the total quantity of agricultural by products or wastes which are cellulosic in nature accounts for nearly 50–100 million tons per year nearly 50% of which is cellulose (Ghose and Ghose, 1970). The detailed break up of cellulosic wastes available in India has been worked out (Paul, 1981) and is given in table 4. The cost analysis of the recovery of cellulose from various wastes has been done (Dunlop, 1974).

TABLE - 4

Cellulosic Wastes in India

Cellulosic Material	Million tons/annum
Bagasse	5.3
Cotton(stalks, linters etc.)	13.0
Forest wastes(leaves, branches felled trees etc.)	3.2
Jute sticks	2.5
Rice husk	15.0
Rice straw	66.0
Total	105.0

It is amply evident from previous paragraphs that huge amount of cellulosic wastes find way to garbage heap. If used meticulously these wastes may become prime raw materials for further conversion to other products of utility to man. Cellulose recovery and conversion to industrially important compounds can be profitable venture reaping rich dividends. Some work has been done in this direction, but, only surface has been scratched. It requires more intensive research programme.

It is rather unfortunate that man-kind does not possess the biochemical set up that can degrade cellulose into simpler and more assimilable components such as glucose and other sugars, as this could have been an obvious solution to the pressing food problem. Current research effort in this direction shows promise for the conversion of cellulose to single cell protein, raw materials for fermentation and development of cellulosic substrates that can be acted upon by enzymes.

1.6 Pollution:a Menace

Enormous amount of cellulose released at various stages of utilization has caused many handling and storage problems. Burning and dumping in rivers to ease its handling has resulted in air and liquid pollution. Mountains of garbage heaps in urban areas while adding to the solid pollution have made the life miserable. The omnipresent natures gift, cellulose, is however getting erased from the surface of the earth due to over usage and exploitation of cellulosic sources. This while increasing the strain on the ecological balance, has made the planet pollution prone.

In a way, the problem of pollution is not new and is as old as the planet. The genesis of environmental problem dates back to the era of Adam and Eve. It was Adam, history books say, who first polluted this planet with the apple core. Since then the world has been flooded with tons and tons of man made wastes; solid, liquid and gaseous, not to mention of nuclear waste. Recently pollution menace has reached a threatening proportion due to the rapid growth in the field of Science and Technology and industrialisation of life.

Waste anywhere under the sun is a headache, an unending problem and growing pile of garbage. Everyone of us throw our share of waste in the form of newspaper, garbage, cans, bottles and myriads of others without a second thought. We show concern only when the waste is in our own backyard. Today, the problem of waste is not just limited to backyards but has attracted global attention.

Recycling: the solution

Is there a solution to the problem of wastage? How can this waste become a resource? The answer is recycling. Time has come for every individual to think of waste as a potential resource. Recycling has to be our new life style. Recycling societies are being formed all over the world to educate and train people to recycle the waste. Ecologists, Scientists and all others concerned are running from pillar to post to check the pollution menace. As a result new terminologies such as environmental management, waste utilization, pollution abatement and recycling have found place in common parlance.

Today, one has to think twice before throwing anything away. Conservation and recycling can be a boon in these days for all shortages of basic needs. Few men who had the vision to call waste a resource are showing the way not only to control pollution menace but also to make life self-sufficient. Those who had the temerity to consider waste as an useless heap of garbage are changing their opinion, because, recycling may bring relief to environmental pollution problems associated with waste disposal.

Many of the cellulosic wastes (newspaper, agricultural residues etc.) which were originally dumped to pollute the atmosphere are being recycled to make items of utility such as hard boards, sheets, pads, file covers and insulation sheets.

The present thesis deals with the recycling of cellulosic wastes into a commercially important commodity known as MCC. Corncobs, bagasse and newsprint have been investigated as potential raw materials for the purpose.

1.7 Literature Surveyed

Pioneering work in the field of MCC is that of Battista et al (1956, 1961, 1962, 1964, 1970 and 1975), who also coined the term MCC in 1962. MCC is marketed today in several countries under various trade names such as Avicels, Loba-MCC, Acme-MCC etc. MCC is generally prepared from high alpha cellulose of wood pulp.

Recently cheaper cellulosic sources have been used. An in expensive form of MCC was prepared from cotton cellulose and evaluated as a tablet excipient (Baichwal and Gupta, 1975). Preparation of MCC from cotton cellulose through the action of HCl and H_2SO_4 has also been studied (Bose et al, 1972). But hydrolysis with H_2SO_4 resulted in the formation of sulphate ester groups on the surface of the microcrystals (Mukherjee and Woods, 1953). MCC has been prepared from saw dust (Jacopian et al, 1975) by two step cooking with $NaHSO_3$ and aqueous SO_2 followed by multistage bleaching with chlorine, extraction with alkali and bleaching with hypochlorite. Newsprint waste was converted into MCC (Nagavi and Mithal, 1979) by deinking, bleaching, hydrolysis and mechanical disintegration. The recycling of newsprint waste into MCC (Nagavi and Mithal, 1982) was optimized to workout a simple and economical process. The authors compared the MCC so produced from Newsprint waste with marketed varieties. Anand and Chawla (1981) successfully prepared MCC from bleached cotton hosiery waste adopting spray drying method. MCC so prepared conformed to most of the British standards. MCC was also prepared from fast growing Indian plants (Manavalan et al, 1981). Efforts to produce MCC from other agricultural residues such as bagasse and corncob, as discussed in the present thesis, have proved fruitful.

Kamakura and Kaetsu (1978) studied radiation induced decomposition and enzymatic hydrolysis of cellulose, whereas, Duchacek and Bludorsky (1970) investigated the problems involved in the use of irradiation for degradation of cellulose.

Hydrolysis of cellulose and hydrodynamic characteristics of colloidal dispersions have been studied by Marchessault et al (1961), Hermans (1963), Edelson and Hermans (1963) and Battista et al (1971). Rheology of MCC-CMC gels was investigated by Walking and Shangraw (1968). Some hydrodynamic properties of neutral suspensions of cellulose crystalline as related to size and shape were studied by Marchessault et al (1961) and Falkiewicz (1979). Flow behaviour of mixed dispersions of bentonite and MCC used as thickness and binders in suspension dosage forms was studied by Schott (1970).

Crystallinity of the cellulosic materials have been studied by the following methods, X-ray diffraction (Segal et al, 1960, Segal and Conrad; 1957, Lewin et al, 1976). Infra Red Spectroscopy (Nelson and O'Connor, 1964; Moharram and Hakeem, 1980; O'Connor et al, 1958); Isotopic exchange (Sepall and Mason, 1961; Ranby, 1964; Frilette, et al, 1948; Jeffries, 1964; Sumi et al 1964); density measurements (Hermans, 1949); water absorption (Valentine, 1956) and iodine absorption (Daruwalla and Shet, 1962). Middleton and Sanders (1951) gave a method for determining whiteness of materials using spectrophotometric technique. It has been observed that grinding of cellulose in vibratory ball mill (O'Connor et al, 1957) and treatment with ethylamine results in decrystallisation of cellulose. Crystallinity and physical characteristics of MCC, effect of grinding on the physical and chemical properties of medicinals, structure of ground MCC, retention of volatile materials by

MCC and infrared spectra of medicinals in ground mixtures have been thoroughly investigated by Nakai et al (1977 and 1978).

Effect of compression on particle size, distribution surface area, disintegration and dissolution of tablets containing MCC and other materials was studied by Sixsmith (1977). Particle size, densities, angle of repose and tênsile strength of MCC have been computed by Crooks et al (1977),Parera (1977), Marshall et al (1972) and Marshall and Sixsmith (1976). Comparative evaluation of various excipients such as avicel (MCC), Elcema-700 (Micro Fine Cellulose), STA-Rx 1500 (starch) was done by Lerk et al (1974). Bothius et al (1973) compared MCC, starch, lactose, amylose and calcium phosphate for direct compression. Denola et al (1973) investigated the binding activity of some adjuvants (MCC, CMC, lactose, ethyl cellulose, acacia, etc.) and their influence on granular and tablet properties. The effect of compressional pressure on the disintegration of tablets containing MCC was studied by Modella (1974). Marshall et al (1975), Khan and Rhodes (1975), Shotton (1976), Selmeczi et al (1976), Chamlers et al (1976), Grat and Sakr (1978) and Haynor and Steurnegal (1978), who concluded that disintegration of the tablets were pressure dependent and hence dissolution of the active ingredient varied with pressure. Schwartz and Bavitz (1976) studied the dissolution profile and tablet- characteristics of timolol maleate, idomethacin, amitryptyline and hydrochlorthiazide tablets prepared by direct compression with MCC. Comparative evaluation of lubricants added to excipients for direct compression was carried out by Delattre et al (1976) and Augsberger and Shangraw (1966). Intestinal absorption of ground mixture of chloramphenicol palmitate with MCC was investigated by Yamamoto et al (1977). Esezobes and Pilpel (1977) investigated the effect of gelatin and moisture on the interparticle attractive forces and compression behaviour of oxytetracycline tablets containing MCC and alginic acid. The penetration of isooctane and water into tablets of MCC, spray dried maltose, dextrose and their blends was investigated by Lerk et al (1979) and drug permeation through membranes, interaction of common excipients, by Lowering (1976). It was noted that MCC confers maximum stability to formulations. The effect of lubricants and glidants (including MCC) on color stability of Vitamin C tablets was studied by reflectance measurements (Wartz, 1967). Richman et al (1965) used MCC to prepare glyceryl trinitrate sublingual tablets. The bioavailability of the tablets, was noted to be comparable to commercially available hypodermic tablets. The release of amphetamine and sodium phenobarbitone from tablets containing MCC was found to be excellent by Reier and Shangraw (1966).

Spheronization of MCC to improve its flow and other characteristics has been successfully carried out. Miyake et al (1973) spheronized MCC, lactose, and cornstarch using distilled water as the binder. MCC is generally considered as safe (Avicel Bulletin, pH-6). The toxicity studies carried out on animals indicated that it was devoid of teratogenicity and embryo toxicity (Ferch, 1974).

FMC (Food and Machinary Corporation), USA markets various grades of MCC (table-5) to meet different requirements such as direct compression, flow improvement, suspension stability and so on.

TABLE-5

Various Grades of Avicel

Sl. Type No.	Characteristics	References
1.Avicel pH101	P.S-50,M-5% direct compression grade	Avicel pH-6,Bull. -"- RC-34 -do-
2.Avicel pH102	P.S-90,M-5% large p.s for flow improvement	Avicel Rc-34,Bull.
3.Avicel pH103	P.s-50,M-3% low moisture grade	-do-
4.Avicel pH105	p.s.20, M-6% filler	-do-
5.Avicel Cl 611	MCC+12-16% Na CMC M-6%,suspension grade	Avicel RC-56 Bull. -do- RC-60 -do-
6.Avicel RC 581	MCC+11% Na-CMC M-6%,suspension grade high shear required for dispersion	Avicel RC-581Bull.
7.Avicel RC 591	MCC+11% Na- CMC, M-6% suspension grade,low shear will disperse	Avicel Rc-591 Bull.

P.S. - practice size in microns
M - Moisture content

1.8 Problem Delineated

The present project was started with the following four-fold objectives:

1. To produce MCC economically
2. To evolve a method to convert cellulosic wastes such as corncobs, bagasse and newsprint into good quality MCC comparable to marketed varieties.
3. To workout a process for small scale industrial sector.

FMC, Corporation USA markets MCC for commercial purposes under the trade name of 'Avicel'. In USA, 90% of the marketed formulations have Avicel as the additive. But in India, due to the non-availability of good grade MCC, high cost of the available MCC and very high price of imported Avicel, MCC finds limited use. Lack of awareness of the qualities of MCC and its advantages over other additives, may be one of the reasons for its under use in the pharmaceutical and other industries. The present efforts were directed towards economical production of MCC from the available, cheaper and renewable resources.

The comparative [illegible] costs of MCC available in India are given in table 6. The cost of MCC mainly depends on the cost of raw material, extent of conversion, recovery of chemicals and by products, production cost and automation.

TABLE-6

COST OF MCC

MCC type	Approx. cost/kg Rs.	References
MCC - Loba	280	-
Acme - MCC	150	-
MCC- JT Baker	620	-
MCC- CPI	21	-
MCC-RRL-JM	16	Anand and Chawla (1981)

MCC-CPI-MCC, Cellulose Products of India
MCC-RRL-JM-MCC, Regional Research Laboratory, Jammu
(Prepared from hosiery waste)

The study was aimed at working out a scheme for the manufacture of MCC from cellulosic wastes commercially at a cheaper rate. The scheme while producing cheaper MCC was thought to bring relief to the pollution problems of cellulosic wastes. And the ultimate objective was to work out a process suitable for small scale industrial sector so that "cottage units" can be set up to recycle the cellulosic wastes.

Objective was also to test the suitablity of MCC'S so prepared from wastes, as an additive in solid dosage forms like tablets and capsules, and evaluate the dosage forms for physical and biopharmaceutical qualities. In the course of the study, an attempt was to be made to identify the products of hydrolysis and see whether any component of the hydrolysate, which accounts for about one-fourth of the cellulose molecule, can be simultaneously won as a by-product in the conversion of cellulosic wastes into MCC.

CHAPTER - II

Proximate Analysis of Cellulosic Wastes

The proximate analysis of cellulosic wastes was undertaken to determine the amount of cellulose, non-cellulosics and other impurities. The analysis of cellulosic wastes helps to determine the potential of the waste for recycling on the one hand and to work out a strategy to get rid of the unwanted non-cellulosic components on the other.

Various methods appear in the literature for the proximate analysis of cellulosic wastes. Important components analysed were holocellulose, alpha cellulose, pentosans, lignin, ash etc. Amongst the methods available for the analysis, TAPPI (Technical Association for Pulp and Paper Industries, 1968) methods are widely used, due to their simplicity and economical analysis with least sophistication in terms of instruments. Most of the analytical methods discussed in TAPPI (1968) are titrimetric or gravimetric. However the range of experimental errors is more. Since the quantum of analysed materials like cellulose, lignin, pentosans etc. is high, the errors become comparitively insignificant. That is the justification for the term Proximate Analysis.

A potentiometric method is discussed in the literature (Launer, 1963) for the determination of cellulose content. But the method has a serious draw-back. For example, small amounts of lignin, pentosans and other carbonaceous compounds if present with cellulose can interfere, as they also get oxidised with cellulose giving very high results. Browning (1967a) has discussed various methods for the isolation of holocellulose.

TAPPI (1968) methods were followed in the present work for the analysis. Holocellulose (total carbohydrate content) was estimated by acidified chlorite method in which chlorinated lignin easily gets separated from holocellulose. The reactions taking place in the acidified chlorite system are temperature and pH dependent. At 60° the following reaction takes place according to White et al (1942).

$$4ClO_2 \longrightarrow 2\ ClO_2 + HClO_3 + HCl + H_2O$$

At 70° and pH-3 following is the pre-dominant reaction (Paulson, 1962).

$$10\ HClO_2 \longrightarrow 5ClO_2 + 2ClO_3 + 3Cl'$$

where as at 95°, the following reaction has been reported, (Heft, 1960).

$$5\ ClO_2' + 2H \longrightarrow 4ClO_2 + Cl' + 2OH'$$

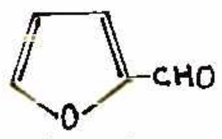
In the above delignitication process some amount of polysaccharides get degraded and lost.

Pentosan alongwith hexosans and cellulosans are generally termed as hemicelluloses. Pentosans mainly yield xylose and arabinose on hydrolysis and form furfural when distilled with 12% HCl. The reaction taking place during distillation is given below, (Browning et al, 1967b)

$$C_5H_8O_4 \xrightarrow{+H_2O} C_5H_{10}O_5 \xrightarrow{-3H_2O} C_5H_4O_2 \text{ or}$$

Pentosan
M.W.- 132.1

Pentose
M.W- 150.1



Furfural
M.W-96.1

The furfuraldehyde so formed may be determined by gravimetric, colorimetric or spectrophotometric methods (Browning, 1967c), TAPPI method, followed in the present thesis involves the precipitation of furfural as phloroglucide with a solution of phloroglucinol followed by drying and weighing. The quantitative relationship that exists between the furfural phloroglucide complex to furfural is used to determine the pentosan content (Page 31).

The general method used for the estimation of lignin involves acid hydrolysis and solubilization of polysaccharides, leaving behind the insoluble lignin which could be determined gravimetrically. The 72% H_2SO_4 used is later diluted and refluxed to complete the hydrolysis. Remaining insoluble material is weighed as lignin. The acid concentration, time of treatment and temperature affect the yield and composition of lignin.

Several solubility tests are carried out to assess the different soluble and insoluble components. Ether solubility is a measure of phytosterols and non-volatile hydrocarbons and to some extent waxes, fats and resins. Solubility in one percent caustic soda indicates the resistance of the cellulosic waste to alkali. It is also a measure of the degree of degradation by fungus or by any other means, because, degradation increases alkali solubility. Ash content is a measure of mineral salts and inorganic foreign matter in the cellulosic waste. It is the residue left behind after ignition at 575±25° for 3 hour or more to burn-off all the carbon.

Actual procedures followed for the proximate analysis of cellulosic wastes are given below

1. Holocellulose (Wise et al,1946)

Moisture free sample (3g) was agitated in a 250 ml conical flask with about 100 ml of distilled water, 2 ml acetic acid and 1 g sodium chlorite and heated on a water bath for about 4 hrs until a white pulp was obtained. Filtered through a weighed glass crucible (G_1 or G_2) and washed with distilled water. Dried at 105° to constant weight.

2. Alpha cellulose (TAPPI, 1968)

Holocellulose (above) was transferred to 250 ml beaker. 75 ml of 17.5% NaOH were added and the admixture kept for 35 minutes. Thereafter 100 ml of distilled water were added and mixture was kept again for 30 min.

Transferred the solution into a tared glass crucible on suction flask and washed with 25 ml of 8.3% NaOH and distilled water to neutral pH. After disconnecting the suction about 15-20 ml of 2N acetic acid was added, and filtration done under suction after a 5 min wait. The residue was washed till free from acid and dried at 105° to constant weight. Absorbent cotton showed maximum and corncobs minimum of alpha-cellulose.

3. <u>Pentosans</u> (TAPPI, 1968)

Known weight of the sample (1.5g) was distilled in a 250 ml round bottom flask with 100 ml of 12% HCl and with a few pumice pieces to avoid bumping. About 400 ml of the distillate was collected in a 500 ml flask through a cotton plug. The volume of the 12% HCl was kept constant in the round bottom flask by addition of more 12% HCl through an adapter separating funnel. Phloroglucinol solution (40 ml) was added to the distillate and allowed to stand for about 16 hrs. The precipitate (furfural phloroglucinol) was collected in a weighed crucible, washed with cold water and dried at 105° to constant weight. The pentosan content was calculated using the following formula

Pentosans = (a + 0.0052) x f

a = Weight of furfural phloroglucide in g
f = 0.895 if a is less than 0.03 g
0.887 if a is between 0.03-0.3 g
0.882 if a is more than 0.3 g

Pentosan content was lowest in cotton and highest in bagasse and corncob. Hence corncob and bagasse could be possible sources of furfuraldehyde.

4. Lignin (TAPPI, 1968)

Accurately weighed sample (1 g) placed in a 250 ml beaker was mixed with 15 ml of 72% cold H_2SO_4. After allowing the solution to stand for 2 hrs it was transferred to a one litre round bottom flask with (560 ml) distilled water (3% acid). It was then refluxed for 4 hrs, cooled, filtered into a weighed crucible, washed free of acid and dried at 105° to constant weight. Lignin was found to be highest in saw dust (36%) and jute straw (32.9%), moderate in other agricultural residues, 11.5% in corncobs, and lowest in cotton (0.01%). Saw dust and jute straw can be potential sources for lignin or lignin based products such as vanillin. Corncobs having little lignin could be handled with ease for cellulose isolation. Hence, corncob has been extensively investigated for MCC preparation.

5. Alcohol- Benzene Extract (TAPPI, 1968)

Accurately weighed sample (2g) was extracted in a Soxhlet apparatus with (200 ml) alcohol-benzene (1:2) mixture for 6-8 hrs. The solvent was distilled till the volume was 1/10th of the original and transferred to a (100 ml) weighed conical flask. After removing the solvent on a water bath, conical flask was dried at 105° to constant weight.

6. Ether Soluble Extract (TA PI, 1968)

Insoluble sample, alcohol-benzene extract was further extracted with (200 ml) solvent ether in a Soxhlet apparatus as above. After recovering 9/10th of the solvent by distillation rest was transferred to a tared conical flask, removed ether on water bath and dried at 105° to constant weight.

7. Cold Water Solubility (TAPPI, 1968)

Accurately weighed sample (2g) was mixed with 300 ml of distilled water, kept for 48 hrs, filtered through a tared crucible and dried to constant weight at 105°.

8. Hot Water Solubility (TAPPI, 1968)

Accurately weighed sample (2g) was placed with 100 ml of distilled water on a boiling water bath in a 250 ml conical flask connected to a reflux condenser, for 3 hrs. Transferred to a tared crucible and dried to constant weight at 105°.

9. 1% Sodium Hydroxide Solubility (TAPPI, 1968)

Accurately weighed sample (2g) was placed in contact with 100 ml of 1% NaOH on a water bath for 1 hr. Filtered into a tared crucible, washed with hot water, flushed with 50 ml of 10% acetic acid and again washed with hot water. Dried at 105° to constant weight. Most of the agricultural residues except cotton show high (1%) alkali solubility as high as 50% in case of corncob.

10. Ash (Tappi, 1968)

Suitable amount of the sample (1 g) was burnt in a silica crucible on a burner and ignited at 575±25° to constant weight. Ash was maximum in corncob and minimum in cotton and newsprint. High content of ash, indicates the presence of unwanted earthy materials such as sand etc.

11. Loss on Drying

Known weight of the samples (1g) was dried at 105° to constant weight and the difference represented the loss on drying.

All the alpha-celluloses prepared from various cellulosic wastes showed brightness above 90% indicating high grade of the isolated material.

Proximate analysis of cellulosic wastes is given in table 7. Proximate analysis of jowar straw, wheat straw etc. is given in table 8 and of various woods in table 9 for comparison.

TABLE - 7

Proximate Analysis of Cellulosic Wastes

Sl No	Material	Holo cellulose	Alpha-cellulose	Pentosans	Lignin	Solubility in Cold water	hot water	alcohol benzene	ether	1% NaOH	Ash	Loss on drying	Whiteness of alpha cellulose
1	Absorbent cotton	95.00	81.50	1.70	0.01	2.00	3.70	0.80	0.50	2.00	0.10	7.90	90%
2	Bagasse*	-	37.00	28.00	22.00	-	-	-	-	36.00	2.60	-	-
3	Bagasse (pulp)	63.00	44.10	29.50	22.50	5.20	8.00	3.80	0.40	1.30	1.80	5.00	90%
4	Corncobs	81.52	33.00	28.02	11.15	8.70	9.20	2.70	0.20	49.00	2.50	7.90	-do-
5	Jute straw (pulp)	66.00	-	25.60	32.90	5.70	8.20	-	-	40.00	1.75	3.00	-do-
6	Myristica spp**	69.82	-	12.4	22.54	1.85	8.92	2.05	-	11.64	0.18	-	-
7	Newsprint	61.00	38.40	17.30	28.00	4.30	6.80	4.00	0.50	12.50	0.10	6.30	90%
8	Saw dust	52.40	35.50	13.00	36.00	6.40	8.00	-	-	16.70	2.00	8.00	-do-

* Sinha et al, 1971

** Madan and Upadhyaya,1981

TABLE - 2

Proximate Analysis of Various Straw's

(Dhake and Khante, 1980-81)

Sl. No. Material	Holo-cellulose	Lignin	Ash	Solubility in		
				Cold water	Hot water	1% NaOH
1.Cotton stalks	58.32	30.13	12.80	12.10	14.90	24.35
2.Jower straw	64.19	25.10	9.41	14.39	13.38	27.30
3.Rice straw	65.73	18.43	16.60	17.60	20.08	30.33
4.Wheat straw	62.49	24.08	6.80	13.40	18.42	28.22

TABLE- 9

Proximate Analysis of Various Woods

(Doree , 1950)

Sl. No. Material	Cellulose	Pentosan	Lignin	Solubility in Cold water	Hot water	Ether	ne % NaOH	Ash
1. Hickory Cell Bark (*Hicoria ovata*)	56.22	18.22	23.44	4.78	5.57	0.63	19.04	0.69
2. Red wood (*sequoia sempervirens*)	48.45	7.80	34.21	7.36	9.86	1.07	20.00	0.21
3. Tan bark oak (*Quercus densiflora*)	58.05	19.59	24.85	4.10	5.60	0.80	23.96	0.83
4. Western yellow pine (*Pinus ponderosa*)	57.41	7.35	26.65	4.09	5.05	8.52	20.30	0.46

CHAPTER- III

Preparation of MCC from Cellulosic Wastes

MCC was prepared from the following cellulosic wastes; corncob, bagasse and newsprint. In case of corncob and bagasse, the important steps involved in the preparation were, prehydrolysis, multistage bleaching, hydrolysis and mechanical disintegration. While in the case of newsprint the steps were deinking, multistage bleaching, hydrolysis and mechanical disintegration. Detailed procedures followed in case are discussed below.

3.1 Preparation of MCC from corncobs

1. Good quality corncobs were cut into small pieces and wet pulped in sprout Waldron mill.
2. Dry pulp was treated with 0.1% and 10% sodium hydroxide (pre-hydrolysis) separately at solid-liquid ratios of 1 : 5, 1:6, 1:8 and 1:10 for 24 hours.
3. The samples were kept at room temperature (rt) and 75° for 24 hrs.
4. Washed free of alkali and dried.
5. Analysed the pulp for holocellulose, alpha-cellulose, pentosans, lignin and permanganate number (Table 10). Permanganate Number is defined as the number of ml of 0.1N $KMnO_4$ required to oxidise 1 g of the pulp.
6. Bleach requirement was determined on the basis of permanganate number (Britt, 1964).
7. Pulp obtained by the pre-hydrolysis with 1.0% alkali at rt 75° at a solid-liquid ratio of 1:6 was chosen for analysis.

8. Above pulp was subjected to multistage (3 stage) bleaching with sodium chlorite and chlorine dioxide with intermittent 1% NaOH extraction.
9. The pulp so obtained, which was nearly white, was washed free of bleaching agents and air dried.
10. The pulp was then hydrolysed with 0.5N, 1.0N, 1.5N, 2.0N, 2.5N and 5.0N HCl at 105° for 15 minutes. (Table 11), at a solid-liquid ratio of 1:6 and DP was determined to see level off, if any.
11. The contents were washed free of acid and mechanically disintegrated in a waring blender.
12. Milky colloidal solutions were filtered and air dried to get cakes which were powdered to get a free flowing MCC flour.

— Determination of permanganate Number/Kappa Number

Dry prehydrolysed pulp was mixed with (60 ml) distilled water in a (1 litre) beaker with a magnetic stirrer and (20 ml) 4N sulphuric acid was added. More distilled water (500 ml) was added to the mixture along with (20 ml) 0.1N potassium permanganate and mixed with the help of magnetic stirrer. Exactly after 5 min ± 10 secs. (16.6%) potassium iodide (10 ml) and 1% starch (1 ml) were added. The mixture was titrated with 0.1 N sodium thiosulphate to colorless end-point. The difference between $KMnO_4$ added and $Na_2S_2O_3$ consumed gave the volume of $KMnO_4$ utilised (by the sample) which was divided by weight of the sample in gm to get the permanganate (Kappa) Number. Bleach requirement was determined from the following equation.

TABLE - 10

Proximate Analysis of Alkali Treated Corncob Pulp

a) Concentration of alkali soln.- 0.1% Temp- Rt and 75°, Time - 24 hrs.

Sl No. Analysis	Solid Liquid Ratio							
	1:5		1:6		1:8		1:10	
	Rt	75	Rt	75	Rt	75	Rt	75
1.Alpha-cellulose	32.80	33.00	32.20	32.40	32.00	31.50	31.00	30.80
2.Holo cellulose	69.00	71.50	68.00	69.80	69.00	69.40	67.20	66.70
3.Lignin	12.00	11.20	11.50	11.00	11.00	10.60	10.50	10.90
4.Pentosans	25.40	23.20	24.00	23.40	22.00	21.80	20.90	20.70
5.Permanganate number	31.20	28.30	29.20	28.00	28.40	27.30	23.50	27.60
b) Concentration of alkali soln- 1.0%, temp - Rt and 75°, Time - 24 hrs								
1.Alpha cellulose	35.50	33.50	33.80	34.00	34.20	32.00	35.00	34.50
2.Holo cellulose	70.50	56.50	67.40	68.10	68.20	65.80	70.60	70.30
3.Lignin	11.40	11.90	10.90	10.40	10.70	8.60	10.30	7.40
4.Pentosans	23.70	25.00	25.10	21.80	24.40	24.70	22.40	25.00
5.Permanganate number	29.20	23.00	27.80	19.40	22.00	19.00	19.40	18.60

Rt - Room Temperature.

All values are in percent

$$\%\ \text{Bleach requirement} = \frac{\text{Permanganate number} \times 0.355}{\text{factor*}}$$

(* factor obtained from table based on permanganate number).

TABLE - 11

Hydrolysis of corncob pulp at various concentrations of HCl and determination of DP

HCl conc. N	DP
0.5	NAD
1.0	NAD
1.5	410
2.0	320
2.5	280
5.0	190

NAD - No appreciable Depolymerisation

3.2 Preparation of MCC from Bagasse

1. Good quality bagasse (100 g) was cut into small pieces and mixed with 10% -120% sodium hydroxide (based on bagasse) and water (800 ml).
2. The mixture was autoclaved at 130°, 25 psi for about 2 hr's.
3. The contents were filtered, washed free of alkali and the pulp was dried and yield found out (Table 12).

TABLE - 12

Prehydrolysis of Bagasse

Sl No	Batch No. MCC-BITS	Weight of Bagasse	Weight of NaOH, g	Amount of NaOH %	Vol. of water, ml	Temp.	Time hrs	% yield
1	B 8151	50 g	60	120	600 ml	130°C 25 psi	2.0	50
2	B 8152	-do-	5	10	600 ml	-do-	1.5	6[illegible]
3	B 8153	-do-	10	20	-do-	-do-	-do-	56
4	B 8154	-do-	50	100	-do-	-do-	-do-	50
5	B 8155	-do-	20	40	-do-	-do-	-do-	50
6	B 8156	-do-	30	60	-do-	-do-	-do-	44
7	B 8157	-do-	40	80	-do-	-do-	-do-	44

4. Permanganate number was found out and bleach requirement calculated (Table 13).

5. Amount of bleach requirement as chlorine was divided amongst chlorine, sodium chlorite and chlorine dioxide with intermittant alkali (2% NaOH) extraction (Table 14).

6. White pulp so obtained was washed free of bleaching materials and alkali and dried.

7. Pulp was hydrolysed with 2.5 N HCl at 105° for 15 minutes to achieve level-off DP. Product was filtered and washed free of acid. Filtrate was used for sugar estimation and recovery of the by-product.

8. Hydrolysed cellulose was mechanically disintegrated in a waring blender in aqueous state.

9. White colloidal material was filtered, dried and powdered to get free flowing MCC.

10. Some characteristics of MCC prepared from bagasse are given in Table 15.

TABLE - 13

Permanganate Number (P.N) of Prehydrolysed Bagasse, pulps

Sl No. Batch Nos Analysis	MCC BITS* B 8151 1	 2
1. Weight of the sample	0.500g	0.4392 g
2. Volume of water	60 ml	60 ml
3. Volume of 4N H_2SO_4	20 ml	20 ml
4. Volume of water	500 ml	500 ml
5. Volume of 0.1N $KMnO_4$	20 ml	20 ml
6. Time of reaction	5 min ± 10 secs	
7. Vol. of KI (16.6%) and starch 1%	10 ml 1 ml	10 ml 1 ml
8. Vol. of 0.1N $Na_2S_2O_3$	15.7 ml	15.5 ml
9. Vol. of 0.1N $KMnO_4$ consumed (5-8)	4.3 ml	4.5 ml
10. P.N.=vol/wt	8.6	10.2
11. Average P.N	9.[illegible]	
12. % bleach requirement as chlorine = PNx0.355/factor*	4.4%	

Sl No.	MCC BITS	PN	Bleach requirement %
1	B 8151	9.3	4.4
2	B 8152	11.4	5.5
3	B 8153	11.2	5.5
4	B 8154	11.2	5.5
5	B 8155	10.0	4.8
6	B 8156	10.4	4.9
7	B 8157	10.0	4.8

* Factor = 0.7515

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*Factor - Pulp and paper manufacture, Vol.1, 1017, 1950

TABLE - 14

Multistage Bleaching of Bagasse Pulps

No. of steps - 4 and 5
Notation - CBCED

Sl No	Batch No. NCC-BITS	Permn. number P.N.	g% Bleach requirement as chlorine	Cl content of stock in %	Weight of pulp, g	Cl$_2$ used			2% NaOH extn			NaClO$_2$ + ClO$_2$(Cl$_2$)			2% NaOH extn			ClO$_2$			Steps	% yield
						Vol. ml	Temp.	Time hr	Vol. ml	Temp o	Time hr	Wt gm	Temp.	Time hr	Vol. ml	Temp o	Time hr	Wt.	Temp	Time hr		
1	B 8151	9.5	4.4	0.30	5	50	rt	0.5	200	70	1	0.2	rt	0.5	200	70	1	0.28	rt	4	5	30
2	B 8152	11.4	5.5	0.30	20	350	"	"	1L	"	1	0.5 50	"	"	1L	"	"	-	-	-	4	33
3	B 8153	11.2	5.5	0.30	20	350	"	"	"	"	"	"	"	"	"	"	"	-	-	-	4	35
4	B 8154	11.2	5.5	0.30	20	350	"	"	"	"	"	"	"	"	"	"	"	-	-	-	4	33
5	B 8155	10.0	4.8	0.43	20	200	"	"	"	"	"	"	"	"	"	"	"	-	-	-	4	30
6	B 8156	10.4	4.9	0.43	20	200	"	"	"	"	"	"	"	"	"	"	"	-	-	-	4	40
7	B 8157	10.0	4.	0.43	20	200	"	"	"	"	"	"	"	"	"	"	"	-	-	-	4	40
8	B 8198	11.2	5.5	0.23	20	650	"	"	"	"	"	0.2	"	"	"	"	"	0.2 20	rt	4	5	36
9	B 8199	11.2	5.5	0.23	20	650	"	"	"	"	"	0.2	"	"	"	"	"	"	"	"	5	40

TABLE - 15

Characteristics of MCC prepared from Bagasse

Sl.Batch No. No.MCC -BITS	Partial size,	DP	Mol. wt.	pH of 12.5% soln.	Loss on drying at 105° %	Bulk density		Angle of repose,°	Yield of %
						A	P		
1.Aiveel pH 101	13.1	236	38,232	6.0	3.0	0.28	0.45	36	-
2. B 8151	11.4	219	35,478	6.0	3.5	0.39	0.60	37	38
3.B 8152	11.2	220	35,640	5.8	3.0	0.39	0.58	36	38
4.B 8153	11.3	221	35802	5.8	3.2	0.39	0.58	36	40
5.B 8154	10.0	220	35640	6.0	3.6	0.43	0.58	42	40
6.B 8155	13.6	240	38800	5.8	4.0	0.29	0.40	36	36
7.B 8156	22.1	290	46980	6.0	4.0	0.40	0.59	39	36
8.B 8157	9.0	220	35640	5.8	3.8	0.42	0.60	43	35
9.MCC-BPC	10.50 um	222	36000	5-7	> 5%	-	-	-	-

A - Aerated

P - Packed

3.3 Preparation of MCC from Newsprint Waste

1. Newsprint (100 g) cut into small pieces was added to (5 litres) hot water and shredded with a powerful mechanical stirrer.
2. Washing soap, surf, (10% of Newsprint) was added and stirring continued for half an hour.
3. The pulp after washing with hot and cold water was dried.
4. Permanganate number was determined to ascertain bleach requirement (Table 16).
5. Five stage bleaching (CECED) was carried out using chlorine, sodium chlorite and chlorine dioxide, 70%, 20% and 10% respectively of the bleach requirement, with intermittant extractions with sodium hydroxide (2% soln.). Milky white pulp obtained was filtered, washed free of chemicals and dried by pressing between a fine cloth and then in oven.
6. The pulp was hydrolysed with 2.5 N HCl for 15 minutes at 105°. Crystalline cellulose obtained was filtered and washed free of acid.
7. Above material was mechanically disintegrated in a waring blender for 10 minutes with dilute sulphuric acid (10 ml).
8. Milky white colloidal suspension obtained was washed and pressed between a fine cloth to remove all the water.
9. Passed through a 16 # sieve to get granular MCC which was dried in air and stored.
10. Several batches were prepared by varying deinking mixture, bleaching agents and hydrolysing conditions (Table 17-22).

11. Granular MCC was powdered and passed through 200 # sieve to obtain a fine powder.
12. Various physical, chemical and pharmaceutical properties of the MCC samples prepared was studied and compared with marketed varieties of MCC (Chapter 4).

TABLE - 16

Permanganate Number of Newsprint

Sl. No	Experimental details	Newsprint
1.	Wt. of the sample, g	0.5
2.	Volume of water ml	60
3.	Volume of 4N H_2SO_4, ml	20
4.	Volume of water, ml	500
5.	Volume of 0.1 N $KMnO_4$, ml	20
6.	Total volume ml	600
7.	Time of reaction min	5
8.	Volume of KI and starch	10 and 1
9.	Volume of 0.1 N $Na_2S_2O_3$, ml	1.7
10.	Blank	20 = 20
11.	Permanganate number	37
12.	% bleach requirement	24

TABLE - 17

Multistage Bleaching of Newsprint Pulp (Batch 1)

1. Sample - Newsprint-pulp (deinked)
2. Initial color - Reddish brown
3. Color after bleaching - light yellow
4. Permanganate Number - 36
5. Bleach requirement - 23.10 %
6. Chlorine content in stock solution - 0.31% Cl'
7. Steps in Bleaching - CEDED (5)
8. Yield - 65%

	1	2	3	4	5
Parameters	Chlorine	2% NaOH H_2O_2	ClO_2	2% NaOH with H_2O_2	ClO_2
1. Wt. of sample	5 g	from 1	from 2	from 3	from 4
2. Volume, ml	200	200	100	200	50
3. Water, ml	-	-	100	-	100
4. Pulp consistency %	2.5	-	-	-	-
5. pH before pulp addition	1.9	12.4	2.0	12.4	1.9
6. pH after addition	1.5	12.4	1.9	12.4	1.5
7. Temp.	rt	60°	rt	60°	rt
8. Time, hr	0.5	1.0	1.0	4.0	12
9. pH of washed solution	7.3	8.3	6.4	7.3	7.3

r.t - room temperature (35°)

TABLE-18

Multistage Bleaching of Newsprint Pulp (Batch 2)

1. Sample - Newsprint pulp (deinked)
2. Initial color - Reddish brown
3. Color after bleaching - Milky white
4. Permanganate Number - 38
5. Bleach requirement - 25.07%
6. Chlorine content in stock -0.6% Cl
7. Steps in bleaching - CECEDEDED (9)
8. Yield - 45%
9. Date 13/5/1980

	1	2	3	4	5	6	7	8	9
Sl. No. Parameters	Chlorine	2% NaOH	Chlorine	2% NaOH	ClO_2	2% NaOH	ClO_2	2% NaOH	ClO_2
1. Sample, wt, g	5.0	from 1	from 2	from 3	from 4	from 5	from 6	from 7	from 8
2. Volume, ml	100	200	100	200	100	200	100	200	50
3. Vol. of water	100	-	100	-	100	-	100	-	150
4. Pulp consistency	2.5%	-	-	-	-	-	-	-	-
5. pH before pulp addition	1.5	12.4	1.5	12.4	1.2	12.4	1.1	12.4	1.3
6. pH after addition	1.5	12.4	1.5	12.4	1.3	12.4	1.1	12.4	1.3
7. Temp.°	rt	60	rt	60	rt	60	rt	60	rt
8. Time, hr	0.5	0.5	0.5	1.0	0.5	1.0	5.0	0.5	10.0
9. pH of washed solution	7.4	9.0	7.6	8.6	7.3	7.6	7.9	8.1	8.0

r.t. = room temperature (33°)

TABLE - 19

Multistage Bleaching of Newsprint Pulp (Batch 3)

1. Sample - Newsprint pulp (deinked)
2. Initial color - pale yellow
3. Color after bleaching - milky white
4. Permanganate Number - 36
5. Bleach requirement - 23.10%
6. Chlorine content in stock solution - 6 g/L
7. Steps in bleaching: CECEDP (6)
8. Yield % - 60
9. Date - 23.11.1980

		1	2	3	4	5	6
Sl No.	Parameters	Chlorine	2% NaOH	$NaClO_2$ & Cl_2	2% NaOH	$NaClo_2$ & Cl_2	2% NaOH H_2O_2
1.	Sample wt.g	20	from 1	from 2	from 3	from 4	from 5
2.	Volume	600 ml	1000 ml	49+ 100 ml	1000 ml	2gm + 50 ml	1000 ml + 50 ml
3.	Pulp consistency	3.0%	3.0%	-	-	-	-
4.	Temp.°	r.t	60	r.t	60	r.t	60
5.	Time,hr	1.0	1.0	1.0	1.0	1.0	1.0

r.t. - room temperature

TABLE - 20

Multistage Bleaching of Newsprint Pulp (Batch 4)

1. Sample - Newsprint pulp (deinked)
2. Initial color - Pale yellow
3. Color after bleaching - silky white
4. Permanganate Number - 56
5. Bleach requirement - 24%
6. Cl_2 content of stock solution - 6g/L
7. Steps in bleaching - CECEDP (6)
8. Yield - 62.5%
9. Date- 6.12.1980

Sl No. Parameters	Cl_2	2% NaOH	$NaClO_2$	2% NaOH	$NaClO_2$ & Cl_2	2% NaOH H_2O_2
1. Sample wt. g	20.0	from 1	from 2	from 3	from 4	from 5
2. Volume, ml	600	1000	4g+HCl 1L H_2O	1000	2g+50 ml +750ml H_2O	1000 ml+ 50 ml
3. Pulp consistency	3.3	3.0	-	-	-	-
4. Temp. °	r.t	60-70	r.t	60-70	r.t	60-70
5. Time, hr	1.0	1.0	1.0	1.0	1.0	1.0

TABLE - 21

Multistage Bleaching of Newsprint Pulp (Batch 5)

1. Sample - Newsprint pulp (deinked)
2. Initial color - Reddish brown
3. Color after bleaching - milky white
4. Permanganate Number - 26
5. Bleach requirement as chlorine - 23.10%
6. Chlorine content in stock solution - 4 g/l
7. Steps in bleaching - CECEDP (6)
8. Yield % - 60
9. Date - 23.05-1980
10. Whiteness - 85%

	1	2	3	4	5	6
Sl. No Parameters	Chlorine	2% NaOH	Chlorine	2% NaOH	ClO_2	2% NaOH + Peroxide
1. Sample, wt, g	5	from 1	from 2	from 3	from 4	from 5
2. Volume, ml	100	200	100	200	100	200+5 ml
3. Water	100	-	100	-	100	-
4. Pulp consistency	2.5	2.5	2.5	2.5	2.5	2.5
5. pH before pulp addition	1.6	11.6	1.6	11.6	1.6	11.6
6. pH after addition	1.5	11.6	1.5	11.6	1.5	11.6
7. Temp. °	r.t	60-65	r.t	60-65	r.t	60-65
8. Time, hr	0.5	1.0	0.5	1.0	0.5	1.0
9. pH of washings	7.3	-	7.3	7.3	7.3	7.3

TABLE - 22

Multistage Bleaching of Newsprint Pulp (Batch 6)

1. Sample - Newsprint pulp (deinked)
2. Initial color - Reddish brown
3. Color after bleaching - Milky white
4. Permanganate Number - 36
5. Bleach requirement - 23.10 %
6. Chlorine content in stock solution -4 g/L
7. Steps in bleaching - CECEDP (6)
8. Yield - 58%
9. Date - 29.05.1980

Sl No. Parameters	1 Chlorine	2 2% NaOH	3 Chlorine	4 2% NaOH	5 ClO_2	6 2% NaOH+ Peroxide
1. Sample, wt, g	25	from 1	from 2	from 3	from 4	from 5
2. Vol. of Cl_2 NaOH	500	1000	500	1000	500	1000
3. Water, ml	500	-	500	-	500	-
4. Pulp consistency	2.5	2.5	2.5	2.5	2.5	2.5
5. pH before adding pulp	1.7	11.7	1.7	11.7	1.9	11.7
6. pH after adding	1.7	11.7	1.7	11.7	1.9	11.7
7. Temp., °	r.t	60-65	r.t	60-65	r.t	60-65
8. Time, hr	0.5	1.0	1.5	1.5	2.0	2.0
9. pH of washed solution	7.3	7.3	7.3	7.3	7.3	7.3

r.t - room temperature (33°)

MCC can be economically produced from corncobs. High cellulose content of corhcobs compared to other agricutural residues resulted in higher yields of MCC. Corncob contained only 11.15% lignin which is much less than the content of other sources, such as saw dust, and jute straw, having 36.0% and 32.9% lignin respectively (Table 10). Removal of lignin and purification was hence a simple task as 3 stage bleaching could* Newsprint waste required 5 stage bleaching (Nagavi and Mithal, 1979) to get pure and white cellulose.

In the preparation of MCC, a solid liquid ratio of 1.6 was found optimum. Since, the viscosity of the suspension, while prehydrolysis, bleaching and hydrolysing, was neither too high nor too low to handle Alkali concentration of 1.0% at room temperature as well as 75° was found satisfactory for prehydrolysis. Other solid-liquid ratio's and alkali concentrations were not satisfactory as either de-lignification was incomplete or too small amount of corncob was handled. Hydrolysis with 2.5 N HCl was satisfactory, since, levelling off was as desired. When 5.0 N HCl was used every crystalline region of cellulose was hydrolysed resulting in lower level-off $\overline{DP}$ (Table 11).

Characteristics of MCC were within official limits (BPC, 1973). Particle size, bulk density, angle of repose, crystallinity and whiteness compared well with other varieties of MCC's (discussed in Chapter 4). It may be stated that, corncob is a cheap and best renewable source for the production

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* yield a pure and white product.

of MCC. As the process is simple and economical cottage units may be set up to recycle corbcobs into industrially important MCC.

Bagasse was converted to MCC. For the prehydrolysis or mercerization, sodium hydroxide, 10%-120% (based on bagasse) was tried, at a solid-liquid ratio of 1:12 and 1:16 at 130° 25 psi for 1.5 to 2.0 hours (Table 12). Alkali concentration of 40% was found satisfactory as it was giving white product. Lower concentrations of [illegible] alkali were giving light yellow product and too high concentrations of the same were dissolving and degrading cellulose. Autoclaving time of 1.5 hrs was found satisfactory. Lower solid-liquid ratio's (1:6, 1:8 and 1:10) which were not tried may also give satisfactory results. Permanganate number (P.N.) is the lowest in case of bagasse (9.3-11.4) amongst the three raw materials studied (Table 13). Higher P.N. in case of corncob and newsprint, may be due to other easily oxidisable carbonaceous materials such as starch, degraded cellulose other than lignin. The fact that corncobs and newsprint have less alpha cellulose when compared to bagasse and more holocellulose in case of corncob shows that it has easily oxidisable materials. Bleach requirement was minimum (4.4%) for bagasse as the P.N. was low. Four and five stage bleachings were tried in case of bagasse and both gave satisfactory results (Table 14). Four stage bleaching will obviously be preferred over five stage bleaching due to economic considerations. Bagasse may also be bleached by 3 stage bleaching, with chlorite, extraction and chlorine dioxide (CED) to get good bleached product. Yield varied from 30%-40%. In all, 7 batches of MCC were prepared and compared the characteristics with avicel pH 101 (Table 15) Particle size, pH of 12.5% solution, bulk density and angle of repose were comparable to standard. In 5 of the 7 batches of MCC prepared, DP is lower (219-220) when compared to standard, avicel pH 101, whose DP was found to be 336. In two batches DP was 240 and 290. Lower concentration of HCl (1.5 N - 2.0 N) may be tried to get slightly higher DP product, from bagasse. Alkaline depolymerisation may be taking place during drastic mercerization and bleaching and thereby reducing the DP of cellulose to a considerable extent. Hence, when hydrolysed with 2.5 N HCl, levelling -off takes place on the lower side of the required range (250-350). Nevertheless, Bagasse is yet another potential source for pure cellulose and cellulose based products. Very easily bagasse could be recycled to produce commercially important commodity,MCC.

The third source that was tried for the preparation of MCC was newsprint waste. Deinking to remove the unwanted ink particles, which are otherwise toxic in MCC, is an extra step required while trying to recycle newsprint waste into MCC. Deinking as discussed in the literature (Duchange, 1963; Solonitsain, 1978; Turai, 1978; and Tamoda, et/al 1978) is a laborious process involving, very costly chemicals, equipment and technical skill. Some methods use soap formed in-situ for removing ink particles, while others use ultra-sonic techniques for ink separation from cellulose fibres. Yet others use sand, glass pieces etc. to expell ink particles from adhering cellulose matrix of newsprint. In the present study, low cost soap (Surf) available in the open market was used to emulsify, engulf and remove ink particles. Surf compared well with synthetic soap, Sodium Lauryl Sulphate (SLS). Mechanical shredding of newsprint in hot water while deinking with surf (10% of newsprint) was effective, economical and simple. Deinked newsprint gave P.N-36 (Table 16). Surf removes ink and other carbon particles along with some water soluble impurities.

Newsprint is actually 80% ground wood and 20% chemical pulp and has many impurities. Multistage bleaching (5-9 steps) was tried with other variations to work out an ideal bleaching process. In the Ist batch (Table 17), 5 steps involving chlorination followed by 2% alkali extraction along with peroxide treatment for simultaneous oxidation and removal of lignin was tried. The product obtained at the end of the 5th stage still had a light yellow tinge, indicating incomplete bleaching. A nine step bleaching (CECEDEED), which took 17 hrs for the full process was also tried (Table 18). At the end of the process, though the product was milky white, yield was substantially less and had taken too long a time. In the other 4 batches, 6 stage bleaching was tried varying several parameters. In the 3rd batch (Table 19), at 3rd stage, $NaClO_2$ and Cl_2 treatment was used, whereas in the 4th batch (Table 20), only $NaClO_2$ treatment was given at 3rd stage. In 5th and 6th batches Cl_2 was used in 3rd stage (Table 21) instead of $NaClO_2$ with varying reaction times at chlorination as well as extraction stages. The pulp consistency was maintained between 2.5%-3.3%, chlorination was generally at ambient temperature, whereas, alkali extraction was at elevated temperature (60-65°). Six stage bleaching (CECEDP, Batch 5, Table 21) was found satisfactory which took minimum time of 4-5 hrs for the whole bleaching process. Yield was about 60% and whiteness of the pulp about 85%. On hydrolysis white newsprint pulp gives crystalline cellulose which on mechanical disintegration in a waring blender gives MCC. Granular MCC may be prepared by passing the mass through a sieve (16 #) and then air drying. Powdered MCC was prepared from granular MCC. Properties of newsprint MCC compared well with standard varieties (Chapter v).

The process of preparing MCC from newsprint- works out costly compared to bagasse and corncob due to additional deinking and rigorous bleaching. Nevertheless, vast amount of newsprint refuge, amply available at throw away price can be converted to MCC, a useful cellulose derivative.

CHAPTER - IV

Controlled Gamma Radiolysis of Cellulose to Produce MCC

Radiation induced depolymerization of cellulose is well documented (Lawton, et al, 1951; Saeman et al, 1952; Charlsby, 1955; Kuna et al, 1972). Wood and ligno cellulosics have been irradiated by gamma radiations from C_o^{60} C_s^{137} Effect of radiation on cellulose has been studied by Beardmore et al (1980) and Nakamura and Kaetsu (1978 and 1979) who reported depolymerization with decrease in crystallinity and increase in digestibility. Ibrahim and Pearce (1980) studied the effect of gamma irradiation on composition and in-vitro digestibility of crop products. Han et al (1981) and Youn and Ciegler (1982) studied the gamma ray induced degradation of lignocellulosic biomass.

A dose of 1 Mrad had no effect on cellulose, while, 10 Mrad or more caused decrease in DP. 500 Mrad made the cellulose water soluble. According to Brenner et al (1979) a dose of 10 Mrad with 0.5% sulphuric acid at 450°F for 15 seconds gave maximum of glucose.widely used sources of gamma radiations are C_o^{60} or C_s^{137} (half-life-30 years). C_s^{137} is a nuclear wasto in power generation and is buried underground. Youn and Ciegler (1982) indicated that C_s^{137} can be a source of gamma radiation in the depolymerisation of ligno cellulosics. Duchacek and Bludorsky (1979) have investigated the risks involved in gamma radiations.

The present investigation was aimed at generation of MCC from cellulosic materials by gamma radiolysis, so that the pollution problems of the agricultural and nuclear wastes could be met. At the same time MCC produced by Gamma radiolysis of cellulose is completely safe as no residual gamma radiations are left in the depolymerized cellulose.

4.1 Gamma Irradiation: Absorbent cotton cellulose was irradiated as such and with 1% alkali in a gamma chamber 900 (BARC, Bombay, India) with Co^{60} as the radiation source Radiation doses were 8.5, 12, 34 and 57 Mrad. Corncob cellulose was irradiated as such, doses being 3.5, 12, 24 and 36 Mrad. Several samples of MCC's were also exposed to gamma radiations with a dose of 8.5 Mrad and degree of Polymerisation, Copper Number, reducing sugars were determined.

The procedures followed for the determination of DP, Copper Number reducing sugars, X-ray diffraction and IR crystallinities are given below:

4.2 Degree of Polymerisation (DP) after Irradiation

TAPPI (1968) method was followed for the determination of DP. The sample (250 mg) was dissolved in cupraethylene-diamine (25 ml) solution and viscosity was measured along with a blank on Rheo Viscometer. Relative viscosity, intrinsic viscosity, molecular weight and average DP were determined. Results are in Table 23.

4.3 Copper Number: TAPPI (1968) method was followed. Hot mixture of Copper Sulphate (5 ml, 10%) and carbonate-bicarbonate (95 ml, 12.9% and 5.0%) solutions were added to the cellulosic sample (1.5 g) and kept for 3 hours on a water bath. Filtered on an ashless filter paper and washed with (100 ml) sodium carbonate solution (5%). Washing was continued with (250 ml) hot water. Cellulose on filter paper was added to (25 ml) molydiphosphoric acid solution. Transferred to a buchner funnel and again washed with cold water till blue molybdenum color was removed. After diluting the filterate to 700 ml, it was titrated with 0.5 N $KMnO_4$ to faint pink color. Copper number was determined from the formula (C.No. = 6.36 x ml $KMnO_4$ x N/W) where N is normality of $KMnO_4$ and W is weight of sample in g. Results to the nearest 0.1 are in Table 24.

4.4 Reducing Sugars: Dinitrosalicyclic acid (DNSA) method was followed. (Peterson and Paoth, 1966). Cellulosic sample (100 mg) irradiated and non-irradiated was dispersed in water (2ml). Sodium hydroxide (3 ml, 3N) and DNSA solutions (3 ml) were added to the above dispersion and diluted to 10 ml. Test tubes were kept in boiling water for 15-30 minutes. Filtered and diluted, if necessary. Absorbance was read at 600 nm. A standard plot of varying concentrations of glucose (0.1 mg/ml-0.4 mg/ml) versus absorbance was made. The standard plot is in figure 3* and the amount of reducing sugars in irradiated and non-irradiated samples is in Table 24.

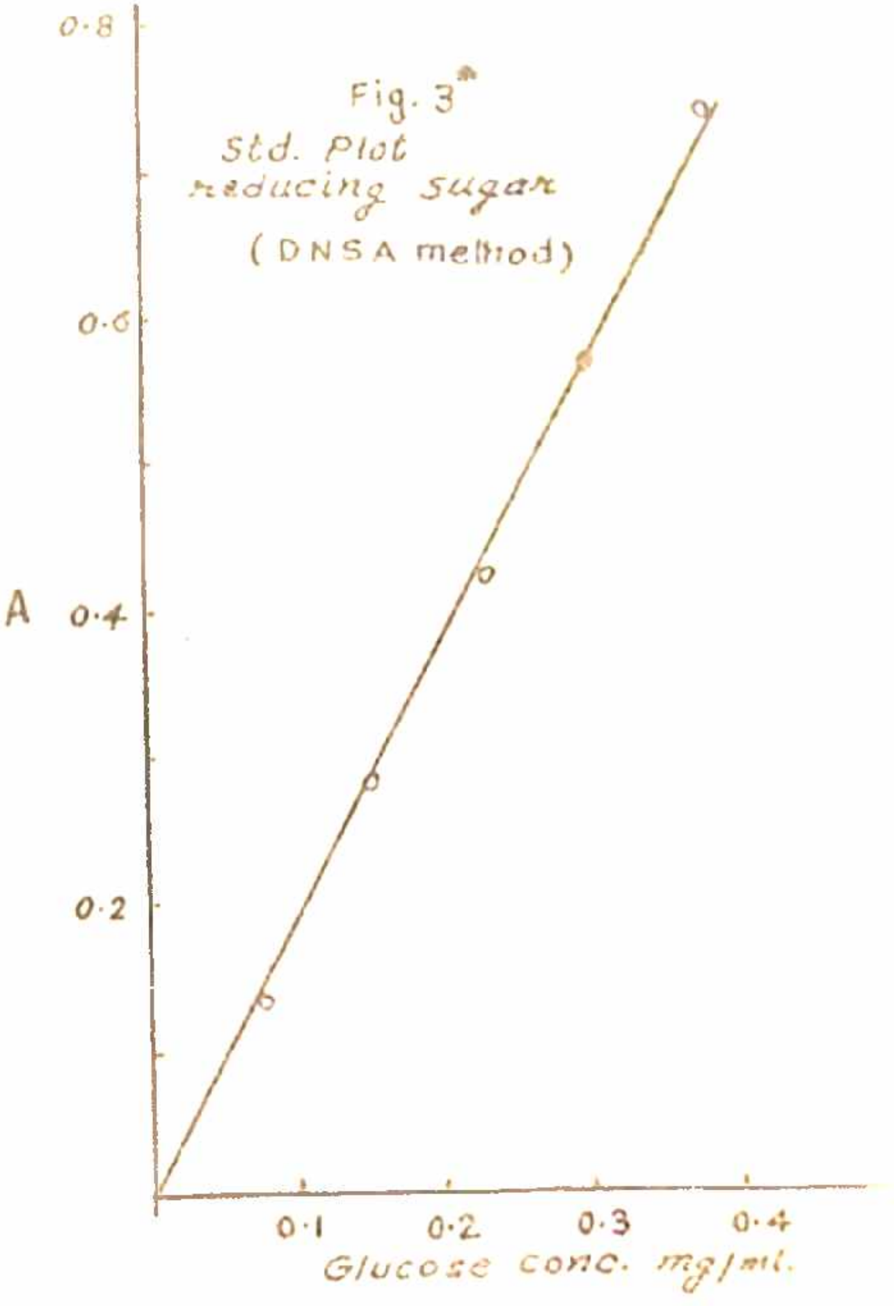

Fig. 3

Std. Plot reducing sugar (DNSA method)

4.5 X-ray Diffraction and Infrared Crystallinities

The method of Segal (1957) was followed, to determine the X-ray diffraction crystallinity indices of irradiated and non-irradiated samples. Crystallinity index was determined by the formula

$$\text{Crystallinity index, \%} = \frac{I_{002} - I_{am}}{I_{002}} \times 100$$

I_{002}- Intensity of crystalline peak (2θ-22.5^{0})
I_{an}- Intensity of amorphous peak (2θ-16^{0})

X-ray diffraction measurements were made on the powder samples on Phillips X-ray powder diffractometer, Model PW 1 50 with nickel filtered CuK_{α} radiations (30 KV, 15 mA). The samples were screened with scanning speed of 2^{0} in 2θ per minute. The ratemeter and the chart speed was kept constant for all the runs. The diffractograms are given in figure 7 and results are in Table 24.

Infrared crystallinity indices were determined by the method of Nelson and O'Connor (1964) taking the ratio of absorption at 1372 cm^{-1} and 2900 cm^{-1}. Infrared spectrograms were taken by KBr disc method on Carl-Zeiss (Zena) Specord 71 IR spectrophotometer. The IR spectrograms are in figure 8 and 9, and results are in Table 24.

TABLE - 23

$\overline{DP}$ of Cotton and Corncob Celluloses Irradiated with Varying Doses of Gamma Radiations

Dose Mrad	Absorbent cotton $\overline{DP}$		Dose Mrad	Corncobs cellulose $\overline{DP}$
	No alkali	1% alkali		
1. 0.0	∽ 2000	∽ 2000	0.0	738
2 8.5	330	259	3.5	721
3 12.0	225	228	12.0	228
4 34.0	108	120	24.0	140
5 45.0	88	75	36.0	97
6 57.0	25	25		

TABLE - 24

$\overline{DP}$, Copper Number, Reducing Sugars, XRD, IR Crystallinities of non-irradiated and irradiated MCC's

Sl Sample No	$\overline{DP}$		Copper Number		Reducing sugars mg/ml		XRD crystallinity		IR Crystallinity	
	B	A	B	A	B	A	B	A	B	A
1.Avicel pH 101	350	195	1.6	2.9	0.27	0.29	82.14	83.57	66.67	73.33
2.Avicel pH 102	282	143	2.3	4.5	0.28	0.30	83.92	85.46	68.88	75.00
3.Acme-MCC	207	154	5.2	7.5	0.30	0.33	85.50	84.25	66.67	63.00
4.MCC-[illegible]L	143	116	3.2	4.2	0.24	0.31	82.14	84.24	75.00	66.67
5.MCC-BITS N 8001	273	157	0.8	2.4	0.13	0.24	-	-	57.14	40.00
6.MCC BITS B 8101	314	195	1.8	4.1	0.28	0.29	85.00	82.06	69.23	71.43
7.Absorbent cotton	~ 2000	330	0.1	1.2	0.30	0.33	-	-	-	-

B = Before Irradiation
A = After Irradiation

XRD - X-ray Diffraction
IR - Infrared

TABLE - 25

Solubility of Cellulose(irradiated) and MCC in alkali

Sl No.	Alkali %	Cotton (non-irradiated)	Cotton (irradiated)	Avicel pH 101	Acme MCC	MCC RRL	MCC BITS Cot 8271
1	1	4.0	8.5 Mrad 15.1	26.6	30.9	32.7	11.0
2	5	5.6	27.9	47.0	52.2	50.2	20.5

Gamma irradiation depolymerises cellulose. Doses between 8.5 Mrad-12 Mrad gave a DP of 200-300. Depolymerised cellulose on mechanical disintegration gives MCC. Depolymerisation of cellulose by gamma irradiation results in new carbonyl group formation as indicated by increase in the sugar content and copper number (Table 24), the increase being dependent on dose. Lower DP at higher doses shows that gamma radiations do not spare the acid resistant crystalline regions. This is due to the high penetrating power of the gamma rays compared to acids. So, levelling off observed in acid hydrolysis is not seen in gamma radiolysis of cellulose as indicated by continuous reduction in DP, with increase of dose (Table 23).

Gamma radiolysis of cellulose increases its solubility in alkali (Table 25). This may be due to formation of lower DP chains, soluble in water and alkaline solutions. In addition, irradiation makes cellulose susceptible to acidic or enzymatic hydrolysis.

CHAPTER - V

Characteristics of MCC

Since the ultimate utility of MCC depends on its characteristics, it is essential to monitor them, so as to infuse the required qualities in the final product. MCC's prepared from waste materials have been compared with commercial varieties in respect of following characteristics:

1. Physico-chemical characteristics

   a. Appearance
   b. Solubility
   c. Loss on drying
   d. pH of 12.5% dispersion
   e. DP and molecular weight
   f. Test for chloride, sulphate and arsenic limits
   g. Particle size
   h. Bulk density (aerated and packed)
   i. Angle of repose
   j. Rheology of MCC, MCC-CMC suspensions

2. Spectroscopic and other Characteristics

   a. X-Ray Diffraction Crystallinity
   b. Infrared Crystallinity
   c. Diffuse Reflectance Spectroscopy
   d. NMR Spectroscopy
   e. Flame photometry for Na, K & Ca content of MCC's
   f. Atomic Absorption spectroscopy for Zn, Cu, Mn and Pb analysis
   g. Differential Thermal Analysis of MCC's
   h. Optical and electron micrographs

In the following paragraphs above characteristics have been discussed in essential detail.

1. Physico-chemical Properties

a. Appearance. MCC is a white, free flowing, and very fine powder. In cases where specially prepared MCC was granular and easily dispersable in water.

b. Solubility: All the samples of MCC were insoluble in water. They were partially soluble with swelling in alkalies and insoluble in acids and most of the organic solvents.

c. Loss on Drying: Accurately weighed (0.5 g) MCC, transferred to a tared (5 ml) conical flask, was dried at 105° for constant weight. Percentage losses on drying were between 3% and 5%.

d. pH of 12.5% Dispersion: MCC (1.25 g) was dispersed in (10 ml) distilled water and pH was read on a calibrated Elico pH meter. Values were found to be between 6.4 and 7.0

e. DP and Molecular Weight: Methods used for the determination of degree of Polymerisation (DP) and molecular weight of cellulose or MCC can be classified into three main types. (Browning, 1967d). These methods correlate variation in physical and chemical properties of cellulose with the average number of anhydroglucose units.

1. Based on thermodynamic analysis
   - a. Osmotic pressure
   - b. Light scattering
   - c. Ultracentrifugation
2. Based on hydrodynamic analysis:
   - a. Viscosity
   - b. Sedimentation velocity
   - c. Diffusion

3. Based on chemical analysis of end groups hydroxyl groups (primary and secondary)

Viscosity method is the simplest and is hence used widely, amongst the methods listed above.

Determination of DP and Mol. wt.

Cellulose or MCC (250 mg) was dissolved in cupraethylene diamine (Cuen, 25 ml). The time taken in seconds for the ball to rundown a known distance for sample (t1) and blank (to) was done on a Rheo Viscosimeter. Relative Viscosity was determined ($\eta_{rel} = t_1/t_0$). Intrinsic viscosity (η) based on relative viscosity was read from the table of ASTM Standards (1966) (Table 26). Molecular weight and DP were determined from standard equations.

$$\text{Mol. wt} = \frac{\eta}{K} \qquad \text{DP} = \frac{\text{Mol.wt}}{162}$$

$$K = 2.5 \times 10^{-5}$$

DP and molecular weight of different celluloses were determined and are given in Table 27.

TEST FOR INTRINSIC VISCOSITY OF CELLULOSE (D 1795)

TABLE 26—INTRINSIC VISCOSITY, $[\eta]c$, AT DIFFERENT VALUES OF RELATIVE VISCOSITY, η_{rel} $^{a, b}$

	$[\eta]c$									
η_{rel}	0.00	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09
1.1	0.098	0.106	0.115	0.125	0.134	0.143	0.152	0.161	0.170	0.180
1.2	0.189	0.198	0.207	0.216	0.225	0.233	0.242	0.250	0.259	0.268
1.3	0.276	0.285	0.293	0.302	0.310	0.318	0.326	0.334	0.342	0.350
1.4	0.358	0.367	0.375	0.383	0.391	0.399	0.407	0.414	0.422	0.430
1.5	0.437	0.445	0.453	0.460	0.468	0.476	0.484	0.491	0.499	0.507
1.6	0.515	0.522	0.529	0.536	0.544	0.551	0.558	0.566	0.573	0.580
1.7	0.587	0.595	0.602	0.608	0.615	0.622	0.629	0.636	0.642	0.649
1.8	0.656	0.663	0.670	0.677	0.683	0.690	0.697	0.704	0.710	0.717
1.9	0.723	0.730	0.736	0.743	0.749	0.756	0.762	0.769	0.775	0.782
2.0	0.788	0.795	0.802	0.809	0.815	0.821	0.827	0.833	0.840	0.846
2.1	0.852	0.858	0.864	0.870	0.876	0.882	0.888	0.894	0.900	0.906
2.2	0.912	0.918	0.924	0.929	0.935	0.941	0.948	0.953	0.959	0.965
2.3	0.971	0.976	0.983	0.988	0.994	1.000	1.006	1.011	1.017	1.022
2.4	1.028	1.033	1.039	1.044	1.050	1.056	1.061	1.067	1.072	1.078
2.5	1.083	1.089	1.094	1.100	1.105	1.111	1.116	1.121	1.126	1.131
2.6	1.137	1.142	1.147	1.153	1.158	1.163	1.169	1.174	1.179	1.184
2.7	1.190	1.195	1.200	1.205	1.210	1.215	1.220	1.225	1.230	1.235
2.8	1.240	1.245	1.250	1.255	1.260	1.265	1.270	1.275	1.280	1.285
2.9	1.290	1.295	1.300	1.305	1.310	1.314	1.319	1.324	1.329	1.333
3.0	1.338	1.343	1.348	1.352	1.357	1.362	1.367	1.371	1.376	1.381
3.1	1.386	1.390	1.395	1.400	1.405	1.409	1.414	1.418	1.423	1.427
3.2	1.432	1.436	1.441	1.446	1.450	1.455	1.459	1.464	1.468	1.473
3.3	1.477	1.482	1.486	1.491	1.496	1.500	1.504	1.508	1.513	1.517
3.4	1.521	1.525	1.529	1.533	1.537	1.542	1.546	1.550	1.554	1.558
3.5	1.562	1.566	1.570	1.575	1.579	1.583	1.587	1.591	1.595	1.600
3.6	1.604	1.608	1.612	1.617	1.621	1.625	1.629	1.633	1.637	1.642
3.7	1.646	1.650	1.654	1.658	1.662	1.666	1.671	1.675	1.679	1.683
3.8	1.687	1.691	1.695	1.700	1.704	1.708	1.712	1.715	1.719	1.723
3.9	1.727	1.731	1.735	1.739	1.742	1.746	1.750	1.754	1.758	1.762
4.0	1.765	1.769	1.773	1.777	1.781	1.785	1.789	1.792	1.796	1.800
4.1	1.804	1.808	1.811	1.815	1.819	1.822	1.826	1.830	1.833	1.837
4.2	1.841	1.845	1.848	1.852	1.856	1.859	1.863	1.867	1.870	1.874
4.3	1.878	1.882	1.885	1.889	1.893	1.896	1.900	1.904	1.907	1.911
4.4	1.914	1.918	1.921	1.925	1.929	1.932	1.936	1.939	1.943	1.946
4.5	1.950	1.954	1.957	1.961	1.964	1.968	1.971	1.975	1.979	1.982
4.6	1.986	1.989	1.993	1.996	2.000	2.003	2.007	2.010	2.013	2.017
4.7	2.020	2.023	2.027	2.030	2.033	2.037	2.040	2.043	2.047	2.050
4.8	2.053	2.057	2.060	2.063	2.067	2.070	2.073	2.077	2.080	2.083
4.9	2.087	2.090	2.093	2.097	2.100	2.103	2.107	2.110	2.113	2.116
5.0	2.119	2.122	2.125	2.129	2.132	2.135	2.139	2.142	2.145	2.148
5.1	2.151	2.154	2.158	2.160	2.164	2.167	2.170	2.173	2.176	2.180
5.2	2.183	2.186	2.190	2.192	2.195	2.197	2.200	2.203	2.206	2.209
5.3	2.212	2.215	2.218	2.221	2.224	2.227	2.230	2.233	2.236	2.240
5.4	2.243	2.246	2.249	2.252	2.255	2.258	2.261	2.264	2.267	2.270
5.5	2.273	2.276	2.279	2.282	2.285	2.288	2.291	2.294	2.297	2.300
5.6	2.303	2.306	2.309	2.312	2.315	2.318	2.320	2.324	2.326	2.329
5.7	2.332	2.335	2.338	2.341	2.344	2.347	2.350	2.353	2.355	2.358
5.8	2.361	2.364	2.367	2.370	2.373	2.376	2.379	2.382	2.384	2.387
5.9	2.390	2.393	2.396	2.400	2.403	2.405	2.408	2.411	2.414	2.417
6.0	2.419	2.422	2.425	2.428	2.431	2.433	2.436	2.439	2.442	2.444
6.1	2.447	2.450	2.453	2.456	2.458	2.461	2.464	2.467	2.470	2.472
6.2	2.475	2.478	2.481	2.483	2.486	2.489	2.492	2.494	2.497	[illegible]
6.3	2.503	2.505	2.508	2.511	2.513	2.516	2.518	2.521	2.524	2.526
6.4	2.529	2.532	2.534	2.537	2.540	2.542	2.545	2.547	2.550	2.553

TEST FOR INTRINSIC VISCOSITY OF CELLULOSE (D 1795)

TABLE 26—INTRINSIC VISCOSITY, $[\eta]c$, AT DIFFERENT VALUES OF RELATIVE VISCOSITY, η_{rel}.[a, b]—(*Concluded*).

	$[\eta]c$									
	0.00	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09
6.5		2.558	2.561	2.563	2.566	2.568	2.571	2.574	2.576	2.579
6.6	2.581	2.584	2.587	2.590	2.592	2.595	2.597	2.600	2.603	2.605
6.7	2.608	2.610	2.613	2.615	2.618	2.620	2.623	2.625	2.627	2.630
6.8	[illegible]	2.635	2.637	2.640	2.643	2.645	2.648	2.650	2.653	2.655
6.9	2.658	2.660	2.663	2.665	2.668	2.670	2.673	2.675	2.678	2.680
7.0	2.683	2.685	2.687	2.690	2.693	2.695	2.698	2.700	2.702	2.705
7.1	2.707	2.710	2.712	2.714	2.717	2.719	2.721	2.724	2.726	2.729
7.2	2.731	2.733	2.736	2.738	2.740	2.743	2.745	2.748	2.750	2.752
7.3	2.755	2.757	2.760	2.762	2.764	2.767	2.769	2.771	2.774	2.776
7.4	2.779	2.781	2.783	2.786	2.788	2.790	2.793	2.795	2.798	2.800
7.5	2.802	2.805	2.807	2.809	2.812	2.814	2.816	2.819	2.821	2.823
7.6	2.826	2.828	2.830	2.833	2.835	2.837	2.840	2.842	2.844	2.847
7.7	2.849	2.851	2.854	2.856	2.858	2.860	2.863	2.865	2.868	2.870
7.8	2.873	2.8	2.877	2.879	2.881	2.884	2.887	2.889	2.891	2.893
7.9	2.895	2.898	2.900	2.902	2.905	2.907	2.909	2.911	2.913	2.915
8.0	2.918	2.920	2.922	2.924	2.926	2.928	2.931	2.933	2.935	2.937
8.1	2.939	2.942	2.944	2.946	2.948	2.950	2.952	2.955	2.957	2.959
8.2	2.961	2.963	2.966	2.968	2.970	2.972	2.974	2.976	2.979	2.981
8.3	2.983	2.985	2.987	2.990	2.992	2.994	2.996	2.998	3.000	3.002
8.4	3.004	3.006	3.008	3.010	3.012	3.015	3.017	3.019	3.021	3.023
8.5	3.025	3.027	3.029	3.031	3.033	3.035	3.037	3.040	3.042	3.044
8.6	3.046	3.048	3.050	3.052	3.054	3.056	3.058	3.060	3.062	3.064
8.7	3.067	3.069	3.071	3.073	3.075	3.077	3.079	3.081	3.083	3.085
8.8	3.087	3.089	3.092	3.094	3.096	3.098	3.100	3.102	3.104	3.106
8.9	3.108	3.110	3.112	3.114	3.116	3.118	3.120	3.122	3.124	3.126
9.0	3.128	3.130	3.132	3.134	3.136	3.138	3.140	3.142	3.144	3.146
9.1	3.148	3.150	3.152	3.154	3.156	3.158	3.160	3.162	3.164	3.166
9.2	3.168	3.170	3.172	3.174	3.176	3.178	3.180	3.182	3.184	3.186
9.3	3.188	3.190	3.192	3.194	3.196	3.198	3.200	3.202	3.204	3.206
9.4	3.208	3.210	3.212	3.214	3.215	3.217	3.219	3.221	3.223	3.225
9.5	3.227	3.229	3.231	3.233	3.235	3.237	3.239	3.241	3.242	3.244
9.6	3.246	3.248	3.250	3.252	3.254	3.256	3.258	3.260	3.262	3.264
9.7	3.266	3.268	3.269	3.271	3.273	3.275	3.277	3.279	3.281	3.283
9.8	3.285	3.287	3.289	3.291	3.293	3.295	3.297	3.298	3.300	3.302
9.9	3.304	3.305	3.307	3.309	3.311	3.313	3.316	3.318	3.320	3.321
	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
10	3.32	3.34	3.36	3.37	3.39	3.41	3.43	3.45	3.46	3.48
11	3.50	3.52	3.53	3.55	3.56	3.58	3.60	3.61	3.63	3.64
12	3.66	3.68	3.69	3.71	3.72	3.74	3.76	3.77	3.79	3.80
13	3.82	3.83	3.85	3.86	3.88	3.89	3.90	3.92	3.93	3.95
14	3.96	3.97	3.99	4.00	4.02	4.03	4.04	4.06	4.07	4.09
15	4.10	4.11	4.13	4.14	4.15	4.17	4.18	4.19	4.20	4.22
16	4.23	4.24	4.25	4.27	4.28	4.29	4.30	4.31	4.33	4.34
17	4.35	4.36	4.37	4.38	4.39	4.41	4.42	4.43	4.44	4.45
18	4.46	4.47	4.48	4.49	4.50	4.52	4.53	4.54	4.55	4.56
19	4.57	4.58	4.59	4.60	4.61	4.62	4.63	4.64	4.65	4.66

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[a] Swedish Method CCA 28:57, Karin Wilson, *Svensk Papperstidning*, Vol. 60, pp. 513 to 521 (1957).

[b] Derived from the equation:

$$\eta_{rel} - 1 = \eta_{sp} = [\eta]c e^{k[\eta]c}$$

where $k = 0.30$

$\overline{DP}$ and Molecular

Sl No	Sample	Time in secs 1	2	3	Mean time t_1	$\eta_{rel} = t_i/t_0$
1	Blank (t_0)	12/13	12/13	12/13	12/13	12/13
2.	Avicel pH 101	38	39	38	38	3.17
3.	Avicel pH 102	22	22	22	22	1.69
4.	Avicel CL 611	24	24	24	24	2.00
5.	Acme-MCC	25	24	25	25	2.08
6.	MCC-CPI	28	28	28	28	2.33
7.	MCC-RRL	23	22	22	22	1.69
8.	MCC BITS NS001	33	33	33	33	2.54
9.	MCC BITS BS101	21	21	21	21	1.75
10.	MCC BITS CS201	27	27	27	27	2.25
11.	Hydrocellulose	26	26	26	26	2.16
12.	Avicel pH 101 (irradiated 8.5 Mrad)	24	24	24	24	2.00

TABLE - 27

Weight of Various MCC's and Celluloses

η	Mol.wt. η /	$\overline{DP} = \frac{Mol.wt.}{162}$
-	-	-
1.418	56,720	350
0.580	23,200	143
0.788	31,520	195
0.840	33,600	207
0.988	39,520	244
0.580	23,200	143
1.105	44,200	173
0.551	22,032	136
0.948	37,908	234
0.888	35,520	219
0.788	31,520	195

Level-off DP of MCC is anywhere between 200-300 depending on the cellulose source, type and extent of hydrolysis. Mild hydrolysis results in lower DP and severe hydrolysis in lower DP.

Cellulose with a basic DP between 2000-3000 gets reduced to one-tenth on hydrolysis. It is perhaps the amorphous region that gets knocked-off leaving behind acid resistant crystalline chains (microfibrils). Stable MCC gels may be prepared by dispersing it in water (5-10% solid content) in a waring blender or a colloid mill.

Generally 2.5 N HCl at 105° for 15-30 minutes is used for hydrolysis. Hydrolysis with H_2SO_4 results in the formation of sulphate ester groups on the surface of the microcrystals and results in changes of its characteristics. Amongst the samples analysed Avicel pH 101 showed maximum DP (350) and MCC BITS B 8101 the minimum (136) and rest in between these two values. Too low DP's in case of Avicel pH 102, MCC-RRL and MCC-BITS B 8101 may be due to severe hydrolysis of cellulose. Molecular weights are determined by multiplying the DP with 162, the mol. wt. of anhydroglucose unit, the building block of MCC.

f. <u>Tests for Chloride, Sulphate and arsenic limits</u>

MCC (2g) was boiled with (20 ml) D. water and filtered and the filtrate (10 ml each) was used for chloride and sulphate limit tests.

<u>Chloride</u>: The filtrate (10 ml) with 1 ml HNO_3 was diluted to 50 ml in a Nesslers Cylinder and (1 ml) $AgNO_3$ (5% ml) was

added and stirred. Opalescence of all the samples was less as compared to standard (0.001 N HCl, 1 ml).

Sulphate: The filtrate (10 ml) with (1 ml) HCl was diluted to 50 ml in a Nesslers Cylinder (10 % 1 ml) $BaCl_2$ was added and stirred. Turbidity was less as compared to standard (0.01 N H_2SO_4, 2.5 ml) for all the samples of MCC.

Arsenic: MCC (5g) was mixed with Na_2CO_3 and Br_2 solution (10 ml) and evaporated on a water bath. Residue was gently ignited and brominated HCl (16 ml) was added with (45 ml) water. Excess bromine was removed by addition of (2ml) stannous chloride solution.

The apparatus and other reagents used were as given in BPC (1979). The above solution was transferred to arsenic apparatus having $HgBr_2$ paper instead of $HgCl_2$ paper. HCl (15 ml), pot. iodide (5ml) and Zinc (5 g)were added. After 2 hrs. no stain was produced in samples of MCC, as compared to standard in which stain was observed.

Chloride, sulphate and arsenic were within official limits for all MCC samples.

g. Particle size

Particle size of MCC may be determined by sieving, optical microscopy, sedimentation, coultercounter and electron microscopy. The last two methods give accurate results with high reliability and reproducibility. Electron microscope apart from determining the particle size, helps to study the surface texture of the MCC's. Coulter-counter was used in the present study for particle size analysis.

The coulter-counter determines the number and size of particles suspended in an electrically conductive liquid. This is done by forcing the suspension through a small aperture having an immersed electrode on either side (Fig.4). The resistance between the two electrodes is altered as particle passes through the aperture. This produces a voltage pulse of short duration having a magnitude proportional to particle volume.

A controlled external vacuum initiates flow from the beaker through aperture and unbalances the mercury siphon. The advancing mercury column makes contact with start and stop probes to activate and inactivate the electronic counter respectively. The probes are placed precisely at 50, 500, and 2000 microlitres away from the start probe thereby providing constant volume for all the counts. In the present work 500 microlitres probe was used. The voltage pulses are amplified and fed to the threshold circuit with an adjustable threshold level. If this level is reached or exceeded by a pulse, it is counted. The threshold level is indicated on an oscilloscope screen by a brightening of the pulse segments, above the threshold, facilitating the selection of appropriate counting levels.

By taking series of counts at selected threshold levels, data is directly obtained for plotting cumulative frequency versus particle size. Integration of all or part of the resultant curve provides a measure of the particle content of the

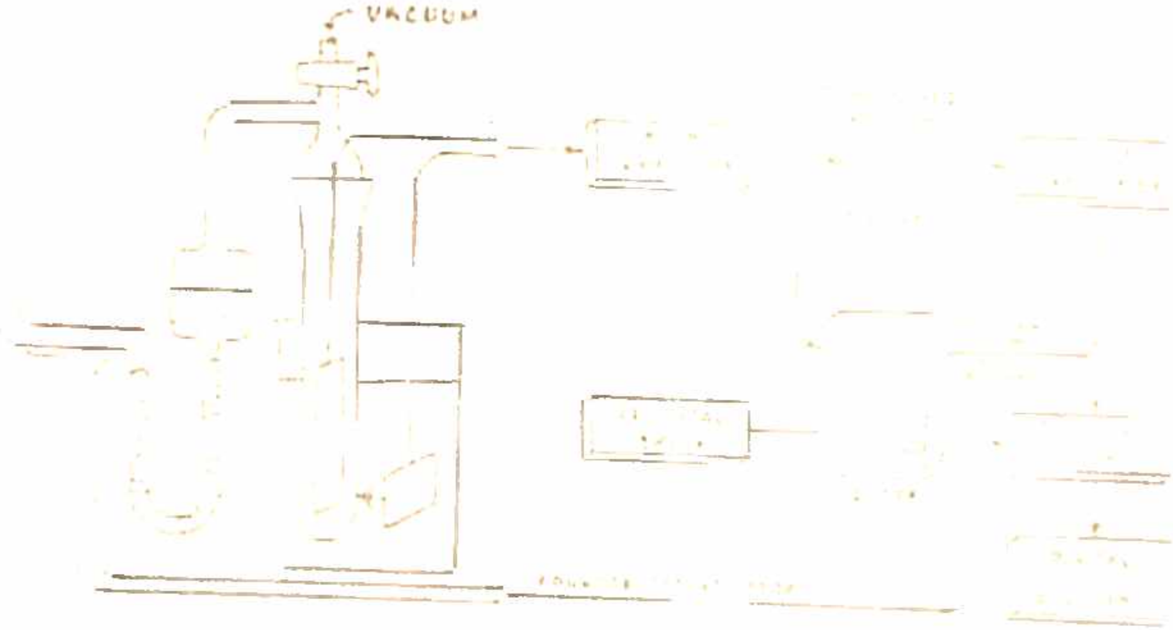


FIG 4 COULTER COUNTER

suspension. The counts are corrected for coincident particle passages (doublets, triplets etc.) and large number of particle counts keeps the statistical deviation low.

The instrument was calibrated with paper mulberry pollens of known particle size and calibration factor determined. The various samples of MCC's were analysed for average particle size distribution. Tables 28-30 give particle size analysis.

Particle size of MCC may be anywhere between 10 microns to 100 microns (B.P.C., 1979) and is a controllable characteristic. It depends on source, method of prehydrolysis, hydrolysis, method of size reduction etc. MCC prepared from bagasse showed lowest particle size (11 microns) and Avicel CL-611 had particle size of 35 microns. Hydrocellulose also had a particle size of 35 microns. Hydrocellulose differs from MCC only with respect to mechanical disintegration. MCC of lower particle size may be used for direct compression and MCC of higher particle size may be used for flow improvement of the fine powders.

h. Bulk density: Bulk density is the weight of the sample present per unit volume (gm/cc). Two types of bulk densities are generally measured - aerated and packed, the former for the loose and latter for the tightly packed samples without voids.

Known weight of the sample (1 g) was transferred to a (10 ml) measuring cylinder and the volume noted. The cylinder was tapped on the table till the volume became constant.

TABLE - 28

Particle Size Analysis by Coulter Counter (CALIBRATION)

Sample - Paper Mulberry pollen
Ap.dia - 140 microns
Ap.Resistance - 11,000 ohms
Operator - BGN
Date 20.2.80

Source -
Man. vol. - 500 μl
Mat. switch - 64 H
T_L - Lower threshold
I - aperture current
A- Amplification

Electrolyte - 1% NaCl
Cal-factor - 13.97
Cal- data -
L_2 = 36.6, I = 1 A = 2
for 12.5 microns

Sl No	t_L	I	A	Raw count	Actual count	$V = Kt_L IA$	$\sqrt[3]{V}$	$d = 1.23 \times \sqrt[3]{V}$	di μ	Δn	$\overline{di}$ μ	$\Delta n.\overline{di}$	Av.size μ
1	20	1	64	-	-	16764	25.60	31.49	>31.49	-	-	-	
2	20	1	32	-	-	8941	20.75	25.52	31.49- 25.52	-	28.50	-	
3	20	1	16	-	14	4470	16.47	20.26	25.52-	14	22.89	320.45	
4	20	1	8	-	283	2235	13.07	16.06	20.26-	269	18.17	4887.73	
5	20	1	4	1	3968	1118	10.38	12.77	16.06-	3685	14.43	53174.55	
6	20	1	2	1	15720	559	8.23	10.12	12.77-	11752	11.45	-	
7	20	1	1	5	14622	280	6.54	8.04	10.12-	-	9.08	4643.24	
8	20	1	1/2	13	16364	140	5.19	6.38	8.04-	644	7.21	-	
9	20	1	1/4	37	841	70	4.12	5.07	6.38-	-	5.73	910	
10	20	1/2	1/4	37	19145	35	3.27	4.02	5.07 & below	200	4.55	-	

B.G.Naqvi 80 pH14007, Pharmacy Dept.

$\Sigma \Delta n = 16564$ $\Sigma \Delta n \overline{di} = 63935.48$

TABLE-29

Particle Size Analysis of MCC by Coulter Counter

Sample - Mcc-Acme
Ap.dia- 140 microns
Ap.Resistance -11,000 ohms
Operator - BGN
Date - 20.2.82

Source - Cellulose
Man.vol.- 500 μl
Mat.switch - 64R
[illegible]

Electrolyte - 1% NaCl
Cal-factor - 13.97
Cal- data -
Lt = 35.6, I = 1 A = 2
for 12.5 μ

Sl No.	t_L	I	A	Raw count	Actual count	$V=Kt_LIA$	$\sqrt[3]{V}$	$d=1.23 \times \sqrt[3]{V}$	di μ	Δn	$\overline{di}$ μ	$\Delta n.\overline{di}$	A.size μ
1	40	8	64	-	-	286106	65.69	81.77	above 81.77	-	-	-	
2	20	8	64	-	10	143053	52.30	64.90	81.77-64.90	10	73.34	733.40	
3	20	4	64	-	62	71526	41.41	51.51	64.90 -	52	58.21	3026.72	
4	20	2	64	-	154	35763	32.95	40.65	51.51 -	92	46.24	4250.40	
5	20	1	64	-	385	17882	26.15	32.45	40.59-	231	36.67	8470.77	
6	20	1	32	-	796	8941	20.70	25.76	32.45-	411	29.11	11964.21	
7	20	1	16	-	1462	4470	16.47	20.44	25.76-	666	23.10	15384.60	13.64
8	20	1	8	-	2876	2235	13.08	16.23	20.44-	1414	18.34	25932.76	
9	20	1	4	-	4475	1118	10.38	12.88	16.23	1599	14.56	23281.44	
10	20	1	2	2	6644	559	8.24	10.23	12.88-	2169	9.17	16450.98	
11	20	1	1	7	8438	279	6.53	8.10	10.23-	1794	7.27	12034.85	
12	20	1	1/2	10	10093	140	5.91	5.44	8.1 & below	1655	5.78	9531.40	

B.G.Nagavi 80PH14007, Pharmacy Dept. $\Sigma\Delta n = 11223$ $\Sigma\Delta n\overline{di} = 153132.37$

TABLE - 30

Average Particle Size of Various MCC's

Sl No	Sample	Particle size in microns
1	Avicel PH 101	13
2	Avicel PH 102	25
3	Avicel CL 611	35
4	MCC- CPI	25
5	ACME - MCC	14
6	MCC - RRL	15
7	MCC BITS N 8001	14
8	MCC BITS B 8101	11
9	MCC BITS C 8201	20
10	Hydro cellulose	30
11	MCC BITS N 7931	23
12	MCC BITS N 7932	22

Aerated and packed bulk densities were calculated. The aerated bulk density varied from 0.25 - 0.38 g/cc, whereas, packed bulk density was between 0.37-0.59 g/cc for different MCC samples (Table 31). Higher bulk density of a sample indicates low porosity and close packing of the particles. On the other hand, lower bulk density is a measure of the fibrous nature of the sample. Particle size, porosity and fibrosity affect the bulk density.

i. Angle of repose: It is the angle made by a heap of powder to the base and is expressed as $\theta = \tan^{-1}(H/R)$ where, θ is the angle of repose, H is the height and R the radius of the heap. Angle of repose is a measure of inter-particular friction, which should necessarily be low when the powder flows through a hopper into a die cavity in solid dosage formulations such as tablets, capsules etc.

Sample was allowed to flow through a small funnel (5 cm dia) whose base tip was at known height (H) from the table. When the sample touched the funnel tip, circular area occupied by the sample was marked, and the diameter and radius of the circle (R) calculated. Angle of repose was determined using the equation given above. Angle of repose varied between 45° and 52° for different samples of MCC's (Table 31).

j. Rheology of MCC, MCC-CMC Suspension

MCC alone cannot form a stable suspension, due to its rapid settling property. Hence, it is generally mixed with (12-16%) CMC to get stable MCC-CMC suspensions. While

TABLE -31

Bulk density and Angle of repose of MCC's

Sl No	Sample	Bulk density gm/cc aerated	packed	Angle of respose,o
1	Avicel PH 101	0.27	0.37	45
2	Avicel PH 102	0.38	0.50	48
3	Avicel CL 611	0.30	0.48	47
4	Acme - MCC	0.38	0.59	52
5	MCC-RRL JH	0.32	0.50	45
6	MCC- CPI	0.28	0.40	48
7	MCC-BITS N 8001	0.25	0.37	48
8	MCC-BITS B 8101	0.28	0.42	46
9	MCC-BITS C 8201	0.30	0.50	47
10	Hydro cellulose	0.27	0.45	50

Higher the angle of repose, rougher and more irregular the surfaces and stronger the interparticle friction.

preparing MCC-CMC suspensions, a certain amount of shear is given in a waring blender or a colloid mill to establish the gel structure. During the shear, more MCC is exposed on which CMC gets adsorbed. Equations used in the rheological studies of MCC/MCC-CMC suspensions were,

$n = Tr/Dr$

n - viscosity

Tr - shear stress, dynes /cm^2

Dr - rate of shear, sec^{-1} (obtained from table)

$Tr = Z \times \alpha$

Z - cylinder constant (5.62)

α - reading on the indicator instrument.

MCC (1g) was dispersed in distilled water (100 ml) and subjected to shear in a waring blender for 15 minutes. Colloidal suspension obtained was used for rheological studies on a Rheotest-2, rotational viscosimeter. Carboxymethyl cellulose (CMC, 3g) was dispersed in distilled water (100 ml). The suspension was warmed and mixed in a waring blender to get transparent gel. The dispersion was used for rheological studies.

The dispersion (25 ml) was transferred to a measuring vessel. Measuring system S/S1 with Z = 5.62 was used. The vessel was adjusted under the measuring cylinder. Rheotest-2 was operated on Mode I at gear nos 9a,10a, 11a and 12 a and then in reverse order. The values of α were noted and shear stress (Tr) was calculated for each gear number while increasing and decreasing. Rate of shear (Dr) was read from the table provided with the instrument, for each gear. Rates of shear (Dr) and shear stresses (Tr) for a 3% CMC suspension are given below (Table 32).

TABLE - 32

Rate of Shear Vs Shear Stress for 3% CMC Suspension

Sl No	Gear Number	Rate of shear (Dr)	$\alpha \downarrow$	Shear stress (Tr)	$\alpha \uparrow$	Shear stress (Tr)
1	9a	243.0	18	101.2	17	95.5
2	10 a	437.4	26	146.1	24	134.9
3	11 a	729.0	36	202.3	35	196.7
4	12 a	1312.0	53	297.8	55	297.8

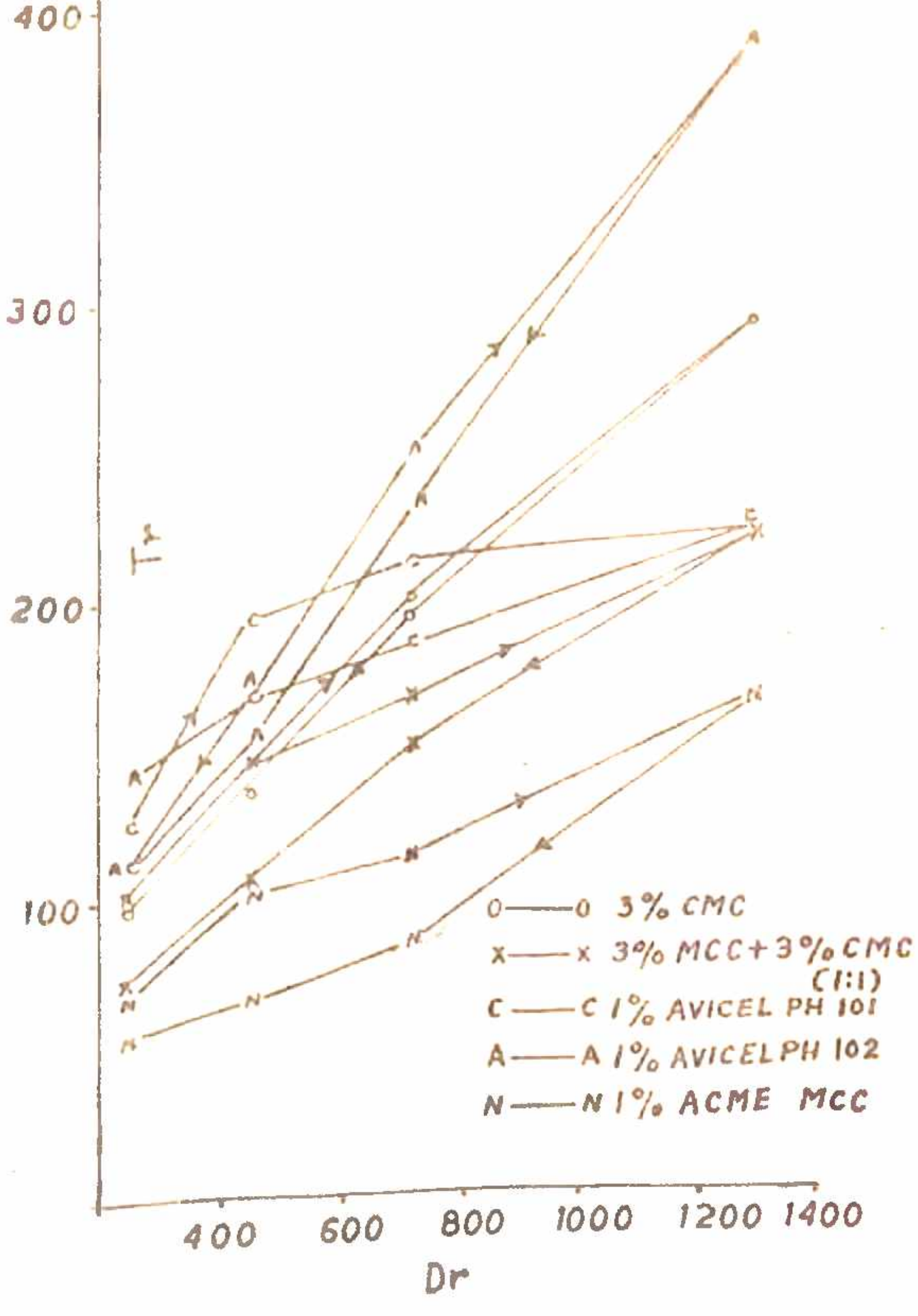
Similar observations were made on Avicel PH 101, Avicel PH 102, Acme -MCC, MCC-CMC suspensions. Rate of shear vs shear stress for various celluloses is given in Fig.(5). Shear stress increased proportionately as rate of shear was increased and avicel PH 102 showed maximum shear strear stress amongst all the samples studied at a rate of shear of 700 sec^{-1} and above. Acme-MCC showed low stress vs strain profile amongst all the samples. Increasing and decreasing rate of shear is indicated by arrow marks showing the direction.

2. Spectroscopic and other Characteristics

a. X-ray diffraction Crystallinity

X-ray diffraction (XRD) measurements were made on the

FIG.5. RHEOLOGY OF MCC, CMC SUSPENSIONS.



powdered samples using Philips X-ray powder diffractometer, Model PW 1350 with nickel Cu-K-alpha radiations (30 KV, 15 mA). The samples were scanned with scanning speed of 2^{o} in 2θ per minute from 2θ 10 to 40. The rate and chart speed were kept constant for all the runs. The diffractograms are given in Figures 6 and 7.

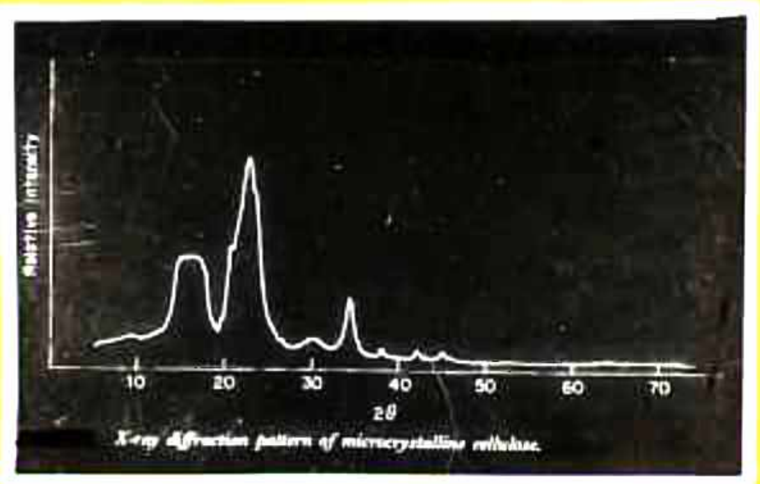
In the X-ray diffractograms of MCC powdered three prominent peaks are noted at 2θ-16, 22.5 and 34. The peak at 22.5 is assigned for crystalline region and one at 16 is assigned for amorphous region. This forms the basis of crystallinity index determination by Segal (1960). However, there was no sharp difference in the X-ray diffractograms of pure cellulose and MCC. In principle, there cannot be a peak for amorphous region of cellulose as XRD is only for crystalline samples. It is presumed that amorphous peak should show a decline and crystalline region a rise in intensity as the ratio of crystalline to amorphous region increases on hydrolysis. This aspect needs further investigation.

X-ray crystallinity indices were determined by the method of Segal and Conrad (1957) and percentage of crystalline material was computed from the relationship given below,

$$\text{Crystallinity Index \%} = \frac{I_{002} - I_{am}}{I_{002}} \times 100$$

I002 = Intensity of Crystalline peak (2θ-22.5^{o})

Iam = Intensity of amorphous peak (2θ-16^{o})



X-ray diffraction pattern of microcrystalline cellulose.

Fig. 6 X-RAY DIFFRACTOGRAM (XRD) OF MCC

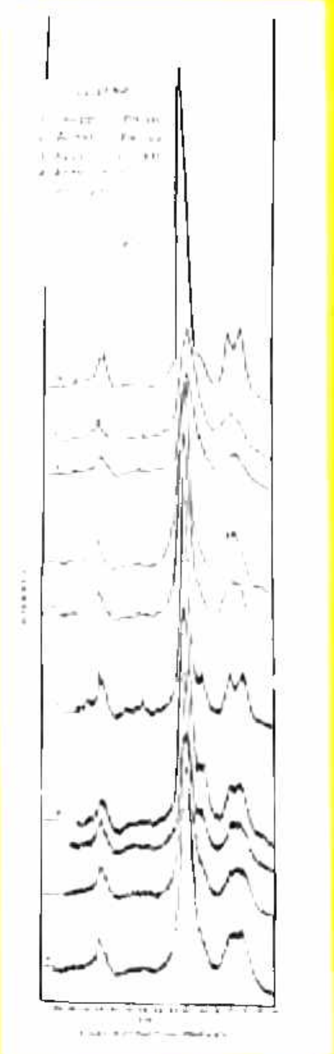
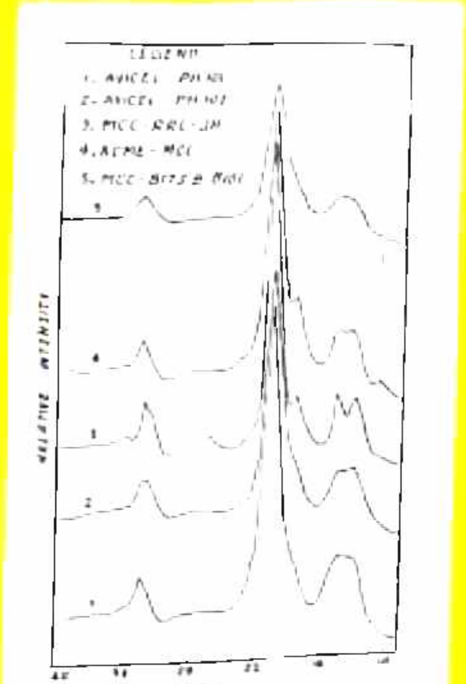


Fig. 7 XRD OF MCC's



X-RAY DIFFRACTION PROFILES OF MICROCRYSTALLINE CELLULOSES IRRADIATED WITH 2.5 MRad GAMMA RADIATIONS

Crystallinity Index %, for different samples of MCC and hydrocellulose, is determined by XRD and Infrared methods are given in Table 33.

TABLE - 33

Crystallinity and Whiteness of MCC's and hydrocellulose

Sl No	Sample	Crystallinity %		Whiteness	Reference
		XRD	IR		
1	Avicel PH 101	83.57	66.67	92	Nagavi et al (1982)
2	Avicel PH 102	85.46	88.88	91	
3	Avicel CL 611	85.00	60.00	90	
4	Acme-MCC	84.25	66.67	86	
5	MCC-RRL	84.24	75.00	89	
6	MCC-CPI	81.25	72.22	83	
7	MCC BITS N 8001	81.20	57.19	65	
8	MCC BITS B 8101	82.86	69.23	81	
9	MCC BITS C 8201	83.56	71.43	71	
10	Hydrocellulose	84.35	92.59	79	

All the samples of MCC showed crystallinity of more than 80%. Avicel PH 102 showed highest XRD crystallinity (85.46%) and MCC prepared from newsprint waste, the lowest (81.20%). Though the XRD method gives only relative set of values, data will be useful in rating a series of samples with respect to one another.

Miller indices (h, k, l values) were calculated for various samples of MCC's and celluloses. Cellulose crystal is a monoclinic system with a= 8.2, b = 10.3, c = 7.9 and B = 82^{o} (Mayer and Misch, 1937). The equation used in the determination of h k values was,

$$\sin^2\theta = h^2\left(\frac{\lambda a^*}{2}\right)^2 + k^2\left(\frac{\lambda b^*}{2}\right)^2 + l^2\left(\frac{\lambda c^*}{2}\right)^2$$

$$+ 2hl\ \frac{\lambda a^*}{2}\ \frac{\lambda c^*}{2}\ \cos\beta^*$$

$$+ 2hk\ \frac{\lambda a^*}{2}\ \frac{\lambda b^*}{2}\ \cos\gamma^*$$

$$+ 2kl\ \frac{\lambda b^*}{2}\ \frac{\lambda c^*}{2}\ \cos\alpha^*$$

where, $a^* = \frac{1}{a \sin\beta^*} = 0.123$

$b^* = \frac{1}{b} = 0.097$

$c^* = \frac{1}{c \sin\beta^*} = 0.127$

$\beta^* = 160 - \beta = 98$

$\sin\beta^* = \sin 98 = 0.99$

$\alpha^* = \gamma^* = 90 = 180 - 90$

$\sin\alpha^* = \sin\gamma^* = \sin 90 = 1$

Bragg's Equation: $n\lambda = 2d \sin\theta$

$$d = \frac{n\lambda}{2 \sin\theta}$$

$$\lambda = 1.542\ A^{o}$$

$\frac{\lambda a^*}{2} = 0.0948$ $\left(\frac{\lambda a^*}{2}\right)^2 = 0.00899$

$\frac{\lambda_b}{2} = 0.0748$ $\quad\left(\frac{\lambda_b}{2}\right)^2 = 0.00560$

$\frac{\lambda_c}{2} = 0.0979$ $\quad\left(\frac{\lambda_c}{2}\right)^2 = 0.00958$

$\cos\alpha = 0,$ $\quad\cos\beta = -0.139,$ $\quad\cos\gamma = 0$

Given below are various values of Sin$^2\theta$ calculated by assigning different hkl values in the above equation

hkl

$101 = 1 \times 0.00899 + 1 \times 0.00958 +$

$2 \times 1 \times 1 \times 0.0948 \times 0.0979 \times -0.139$

$= 0.01599$

$002 = 0 + 0 + 2^2\ (0.00958)$

$= 0.03832$

hkl

$10\bar{1} = 1 \times 0.00899 + 0 + (-1)^2 \times 0.00958 + 2 \times 1 \times -1 \times$

$0.0948 \times 0.0979 \times -0.139$

$= 0.00899 + 0.00958 + 0.00258$

$= \underline{0.02115}$

$103 = 1 \times 0.00899 + 0 + 9 \times 0.00958 + 2 \times 1 \times 3 \times 0.0948$

$\times 0.0979 \times -0.139$

$= 0.09521 - 0.0077402$

$= \underline{0.08747}$

Various values of Sin$^2\theta$'s were determined from the X-ray diffractograms, by making use of θ's at which peaks appeared. Miller indices, calculated and observed, are given in Table 34.

TABLE - 34

Miller Indices (hkl values) of MCC's and cellulose

Sl No.	θ	Sin θ	Sin$^2\theta$ calculated	Theoretical Sin$^2\theta$	hkl	d	I/I1%
1. Avicel PH 101							
1	7°.30'	0.1305	0.01703	0.01599	101	5.93	15.8
2	8,0	0.1392	0.01938	0.02115	$10\bar{1}$	5.54	15.8
3	11,0	0.1908	0.03641	0.03832	002	4.04	100
4	17,0	0.2924	0.08550	0.08747	103	2.64	17.5
2. Avicel PH 102							
1	7° 50'	0.1363	0.01858	0.02115	$10\bar{1}$	5.66	15.6
2	11,0	0.1908	0.03641	0.03832	002	4.04	100
3	17,0	0.2924	0.08550	0.08747	103	2.64	17.8
3. Avicel CL 611							
1	7° 30'	0.1305	0.01703	0.01599	101	5.91	14.0
2	11 10'	0.1937	0.0375	0.03832	002	3.98	100
3	17 ,0	0.2924	0.0 8550	0.08747	103	2.64	16.0
4. Acme - MCC							
1	7°,45'	0.126	0.01588	0.01599	101	6.12	17.2
2	8,00	0.1392	0.01938	0.02115	$10\bar{1}$	5.54	17.2
3	11,00	0.1908	0.03641	0.03832	002	4.04	100
4	17,00	0.2924	0.08550	0.08747	103	2.64	15.5
5. MCC-RRL							
1	7°,15'	0.1260	0.01588	0.01599	101	6.12	16.7
2	8,00	0.1392	0.01938	0.02115	$10\bar{1}$	5.54	16.7
3	11,00	0.1908	0.03641	0.03832	002	4.04	100
4	17,00	0.2924	0.08550	0.08747	103	2.64	18.2

Table 34 continued....

Sl No	θ	Sin θ	Sin^{2}θ calculated	Theoretical Sin2θ	kl	d	I/I1
6. MCC-CPI							
1	7°,30'	0.1305	0.01703	0.01599	101	5.54	19.2
2	8,00	0.1392	0.01938	0.02115	$10\bar{1}$	5.91	19.2
3	11,00	0.1908	0.03641	0.03832	002	4.04	100
4	17.00	0.2924	0.08550	0.08747	103	2.64	15.4
7. MCC-BITS H 8001							
1	7°,30'	0.1305	0.01703	0.01599	101	5.91	15.1
2	8,00	0.1392	0.01938	0.02115	$10\bar{1}$	5.54	15.1
3	11,15	0.1951	0.03806	0.03832	002	3.95	100
4	17,00	0.2924	0.08550	0.08747	103	2.64	13.2
8. MCC BITS B 8101							
1	7°45'	0.1349	0.01820	0.02115	$10\bar{1}$	5.71	16.7
2	11°15'	0.1951	0.03806	0.03832	002	3.95	100
3	17°15'	0.2966	0.08797	0.08747	103	2.60	20.8
9. MCC BITS C 8201							
1	7°45'	0.1349	0.01820	0.02115	$10\bar{1}$	5.71	16.6
2	11°00	0.1906	0.03641	0.03832	002	4.04	100
3	17°15'	0.2966	0.08797	0.08747	103	2.60	20.0
10. Hydrocellulose							
1	7°15'	0.1260	0.01588	0.01599	101	6.12	18.3
2	8°,00	0.1392	0.01938	0.02115	$10\bar{1}$	5.54	16.1
3	11°15'	0.1951	0.03806	0.03832	002	3.95	100
4	17°,00'	0.2924	0.08550	0.08747	103	2.64	10.8
11. Filter paper							
1	7°30'	0.1305	0.01703	0.01599	101	5.93	24.4
2	8°,00'	0.1392	0.01938	0.02115	$10\bar{1}$	5.54	18.9
3	11°30'	0.1994	0.03976	0.03832	002	3.87	100
4	17°00'	0.2924	0.08550	0.08747	103	2.64	6.7
12. Cellulose III							
1	5°50'	0.1016	0.01032	0.01599	101	7.59	-
2	8°40'	0.1507	0.02271	0.02115	$10\bar{1}$	5.12	-
3	10'20'	0.1794	0.03218	0.03832	002	4.30	100

Avicel PH 101, Avicel CL 611, MCC BITS B 8101 and MCC BITS C8201 showed only 3 peaks in their X-ray diffractograms corresponding to 3 different d values (Bragg's equation). Whereas, other MCC's showed 4 peaks corresponding to 4 different d values. In the samples with 3 peaks, reflections were from 101, 002 and 103 planes. While in the remaining ones they were from 101, $10\overline{1}$, 002 and 103 planes. An extraplane $10\overline{1}$ (d- 5.9-6.12), was responsible for reflection corresponding to θ-7°,3' to 7°30'. For the celluloses one sharp and prominent peak appeared at θ 11°15'-11°30' (d-40) corresponding to 002 plane. This was followed by a less prominent peak at 7°30' and least prominent peak at 17°. Theoretical and calculated values of $\mathrm{Sin}^2\theta$ were comparable and hence gave satisfactory hkl values. Filter paper and hydrocellulose also showed 4 planes of reflection corresponding to 101, $10\overline{1}$, 002 and 103 planes, with slight variations in their d values. On the other hand, cellulose III showed only 3 peaks corresponding to 101, $10\overline{1}$ and 002 planes. 103 plane was absent in cellulose III.

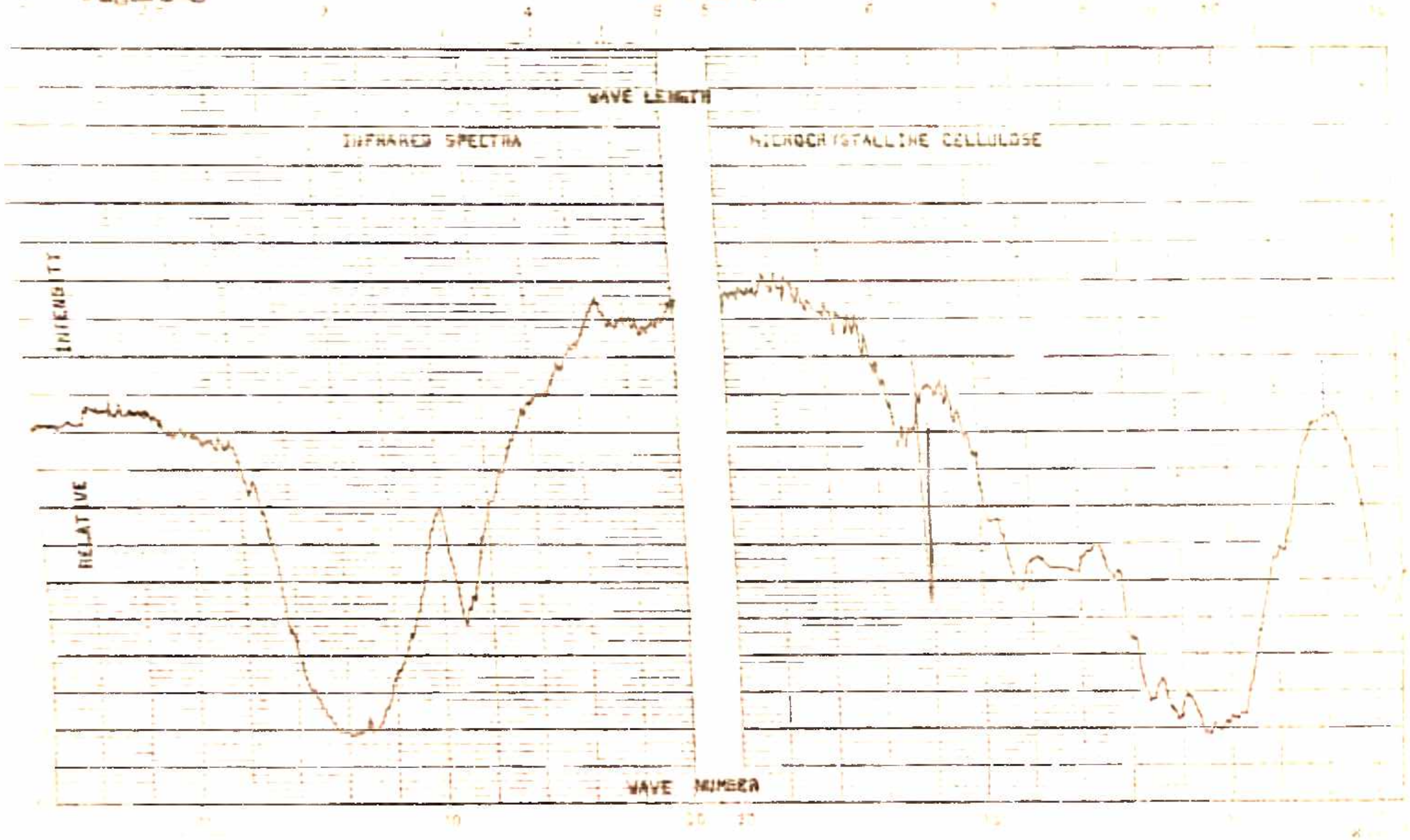
MCC's prepared from cellulosic wastes were comparable to marketed varieties in their X-ray diffractograms, as they gave superimposable plots and similar planes of reflection with slight variations in their d values. But depending on grain size, crystal perfection, orientation, absorption, temperature, sample preparation for XRD, method of preparation of MCC's, small variation in the planes of reflection and hkl values, can occur.

6. Infrared Crystallinity

Infrared (IR) spectrograms were taken by KBr disc method on Carl-Zeiss (Jena) Specord 71, IR Spectrophotometer. The IR spectrograms are given in Fig. 8 and 9.

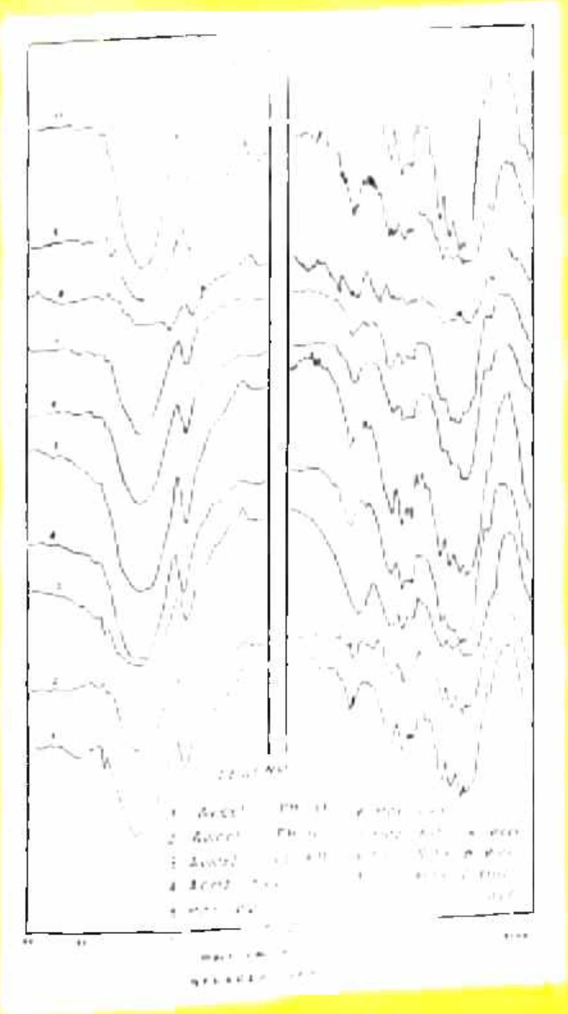
Figure 8 and 9 on next page

In the infrared spectroscopy of celluloses, important frequencies are that of OH groups occuring between 3000-3500 cm^{-1}. Shift in the position of the hydroxyl peaks of a compound in comparison to the parent molecule, indicates structural modifications. Infrared spectroscopy also helps to assess the crystallinity of the sample. Modifications due to H-bonding, chemical and physical agents, polymorphism etc. can also be understood. (Avram and Mateescu, 1970). In raw cotton V_{OH} occurs at 3356 cm^{-1} in cotton linters at 3330 cm^{-1} whereas in chemically modified cotton at higher frequencies. Characteristic peaks for methyl cellulose, ethyl cellulose, cellulose acetate, CMC, cellulose (regenerated from cellulose acetate) and acetylated cellulose appear at 3401, 3425, Figure-8



3
4
5
6
WAVE LENGTH
INFRARED SPECTRA
MICROCRYSTALLINE CELLULOSE
RELATIVE INTENSITY
WAVE NUMBER
10

88f



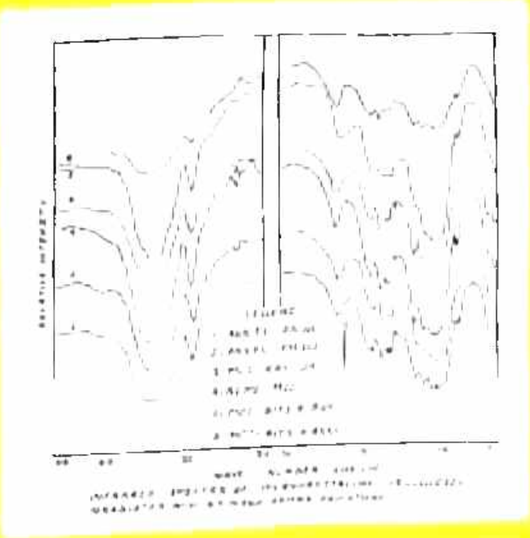


Fig. 9 INFRARED SPECTROGRAM OF MCC's

3497-3509, 3398, 3400 and 3490 cm^{-1} respectively. Deuteration studies help in assessing the degree of crystallinity. Amorphous regions are easily deuterated, whereas, in crystalline region a small change occurs. CH_2 deformation band at 1437 cm^{-1} becomes stronger when the degree of crystallinity increases. It vanishes on breaking. IR spectra shows conversion of CH_2OH of cellulose to COOH (strong peak at 1750 cm^{-1}) and to CHO or C=O (strong peak at 1724 cm^{-1}). Characteristic frequencies in cellulose and MCC with assignment of peaks are given in Table 35.

TABLE- 35

Characteristic Frequencies in Cellulose and MCC

Cellulose frequency cm^{-1}	Vibration
3125-3571	Free V_{OH} and bonded V_{OH}
6131	H_2O
1437	deformation CH_2W
1377	deformation CH
1340	In-plane deformation OH
1319	deformation OH or CH_2W
1285	deformation OH or CH_2W
1247	-do-
1161	Not assigned
1117	-do-
1058	-do-
1030	-do-
829	Deformation CH_2W
MCC frequency cm^{-1}	
3000-3700(3350) B.S	free and bonded OH
2900 S	CH stretching
1675 W	Not assigned
1450 MS	CH_2 W deformation
1350 MS	CH deformation
1000-1200 (1100) S	Not assigned

B.S. - Broad - sharp
W. Weak
M.S. Medium sharp
S. Sharp

The ratio of the peaks at 1449 cm^{-1} and 909 cm^{-1} or 2900 cm^{-1} and 1372 cm^{-1} are used for the determination of crystallinity index. In the present study ratio of the peaks at 2900 cm^{-1} and 1372 cm^{-1} (Nelson and O'Connor, 1964) was used for the determination of crystallinity index, as the peaks at these wave numbers were sharp as compared to peaks at 1449 and 909 cm^{-1}. The results of IR crystallinity index % are given in Table 33 along with XRD crystallinity for comparison. IR crystallinity of hydrocellulose was the highest (92.59%) amongst all samples, and that of MCC prepared from newsprint waste the lowest (57.14%). Since XRD and IR function on different principles, crystallinity obtained by these methods cannot be compared though a relationship can be looked for.

c. Diffuse Reflectance Spectroscopy (DRS)

Whiteness of the powdered MCC samples was measured on varian UV-VIS-NIR (Cary 17 D) spectrophotometer with reflectance attachment against MgO standard at 520 nm. The DRS spectrograms are given in Fig.10.

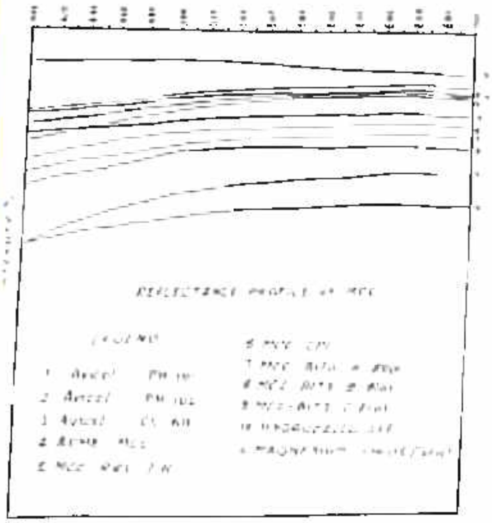


Fig.10 REFLECTANCE PROFILES OF VARIOUS CELLULOSES

DRS showed whiteness above 60% for all samples of MCC. The samples were scanned from 400-700 nm. Avicel PH 101 showed highest brightness (92%) and MCC prepared from newsprint waste (MCC-BITS N 8001) the lowest (65%) against MgO standard (98%). DRS whiteness of various samples of MCC's is given in Table 33.

d. Nuclear Magnetic Resonance Spectroscopy

No work has been reported earlier about the Nuclear Magnetic Resonance (NMR) Spectroscopy of cellulose and MCC, though attempts have been made to study mono, di & tri - saccharides and certain cellulose derivatives (Hall, 1964). Trifluro acetic acid (TFA, CF_3 COOH) was selected as the solvent for the study as it was able to dissolve celluloses.

MCC or cellulose (10-25 mg) was dissolved in a small amount of (1-2 ml) of TFA in a NMR tube. Samples were then analysed on Varian T-60 A(60 MHz) NMR spectrometer, with Tetramethyl Silane (TMS) as the external standard. The NMR plots of various celluloses are given in Figures 11 and 12. MCC-RRL, MCC prepared from newsprint and bagasse waste were irradiated with a dose of 8.5 Mrad gamma radiations and then NMR taken. Results are given in Figure 13.

In all the NMR's two broad peaks appeared at δ 3.6 and the other at δ 4.4 indicating CH_2O and CH proton respectively. OH protons might have been destroyed by TFA or assignment of OH is also to be made against the same two peaks because OH may be overlapping with -CHO protons. OH peaks might have also been

Fig.11 NMR SPECTROGRAMS OF MCC's

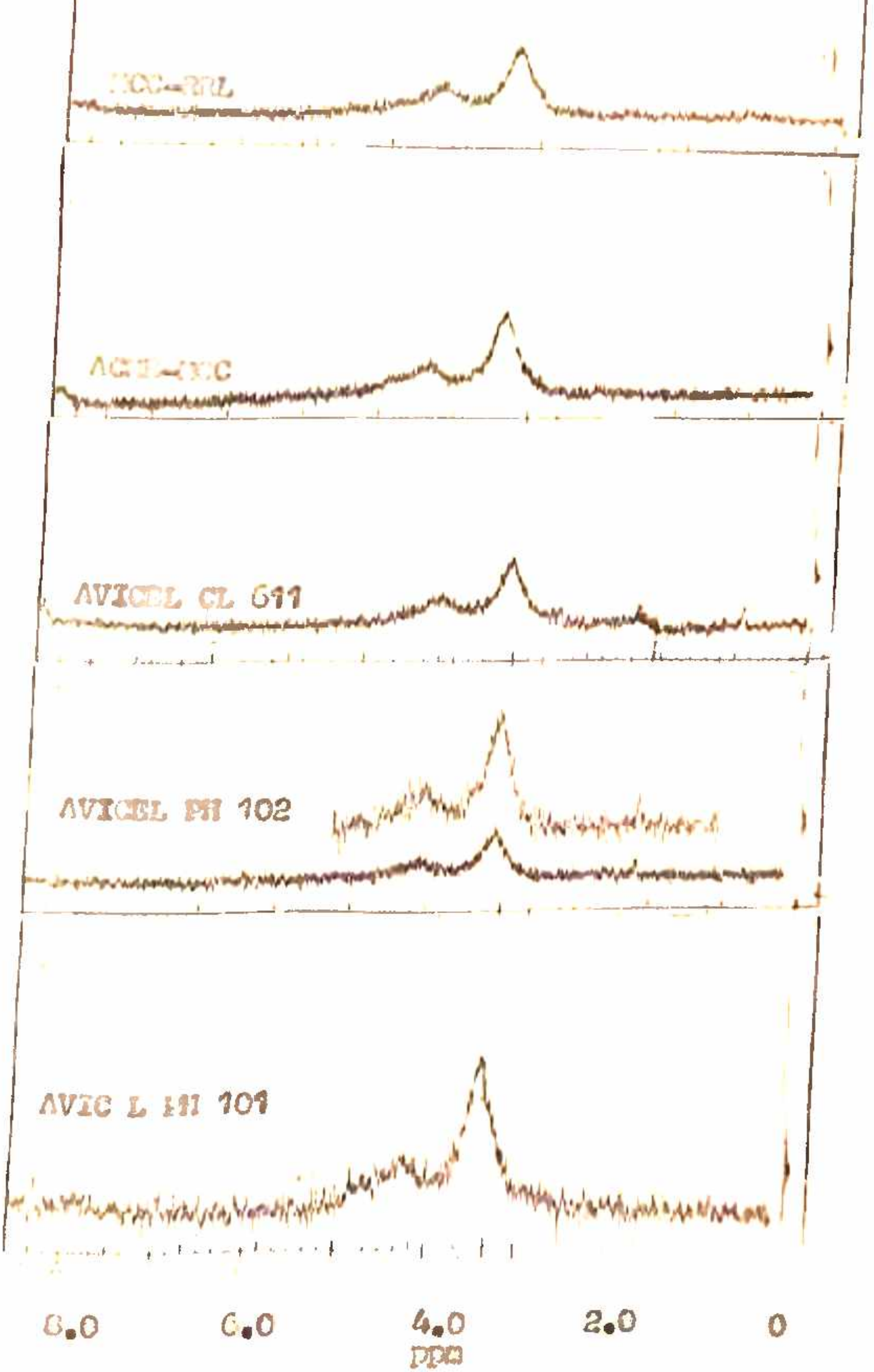


FIG.12 NMR SPECTROGRAMS OF MCC's

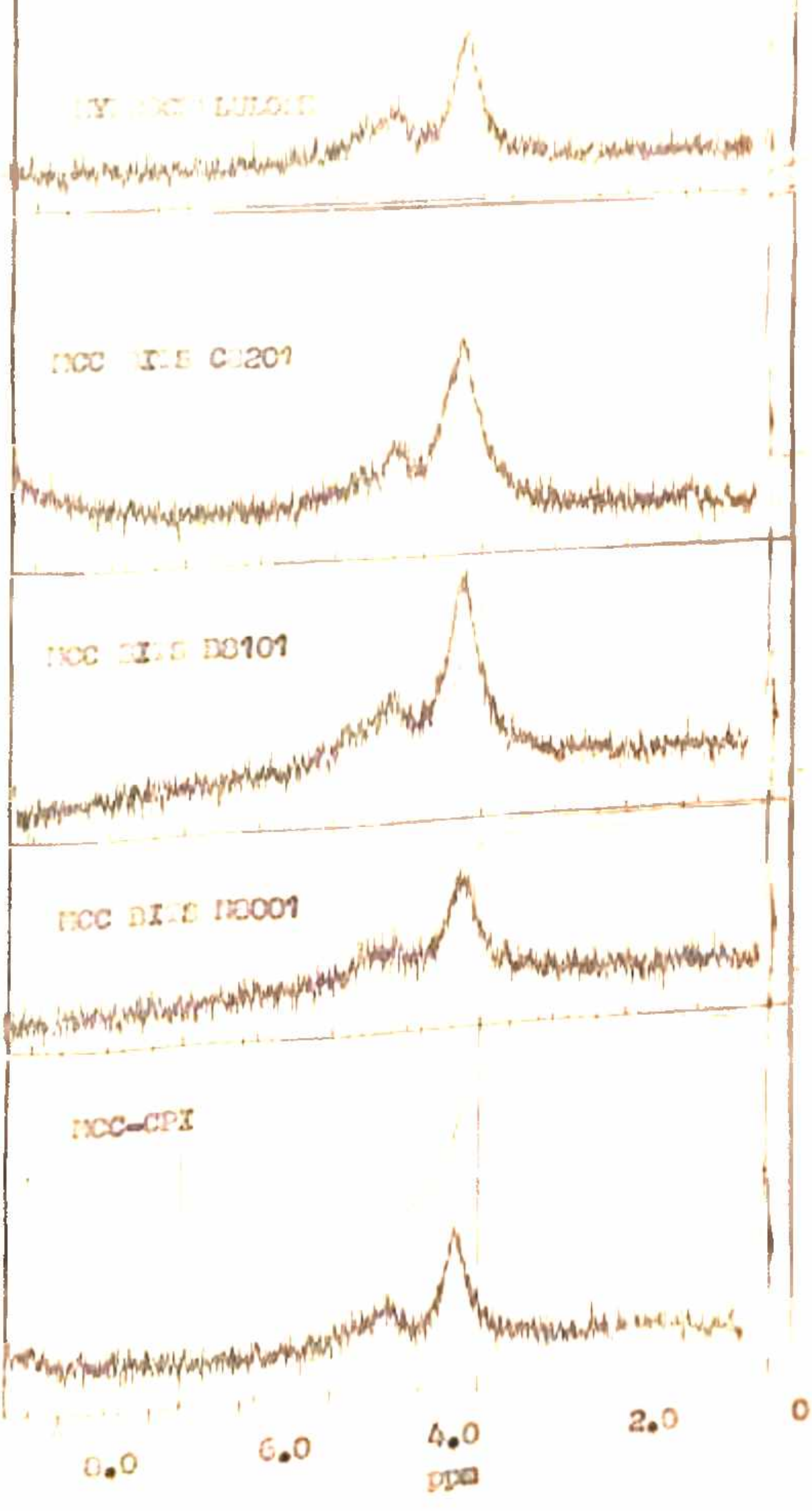


Fig.13 NMR SPECTROGRAM OF IRRADIATED MCC's

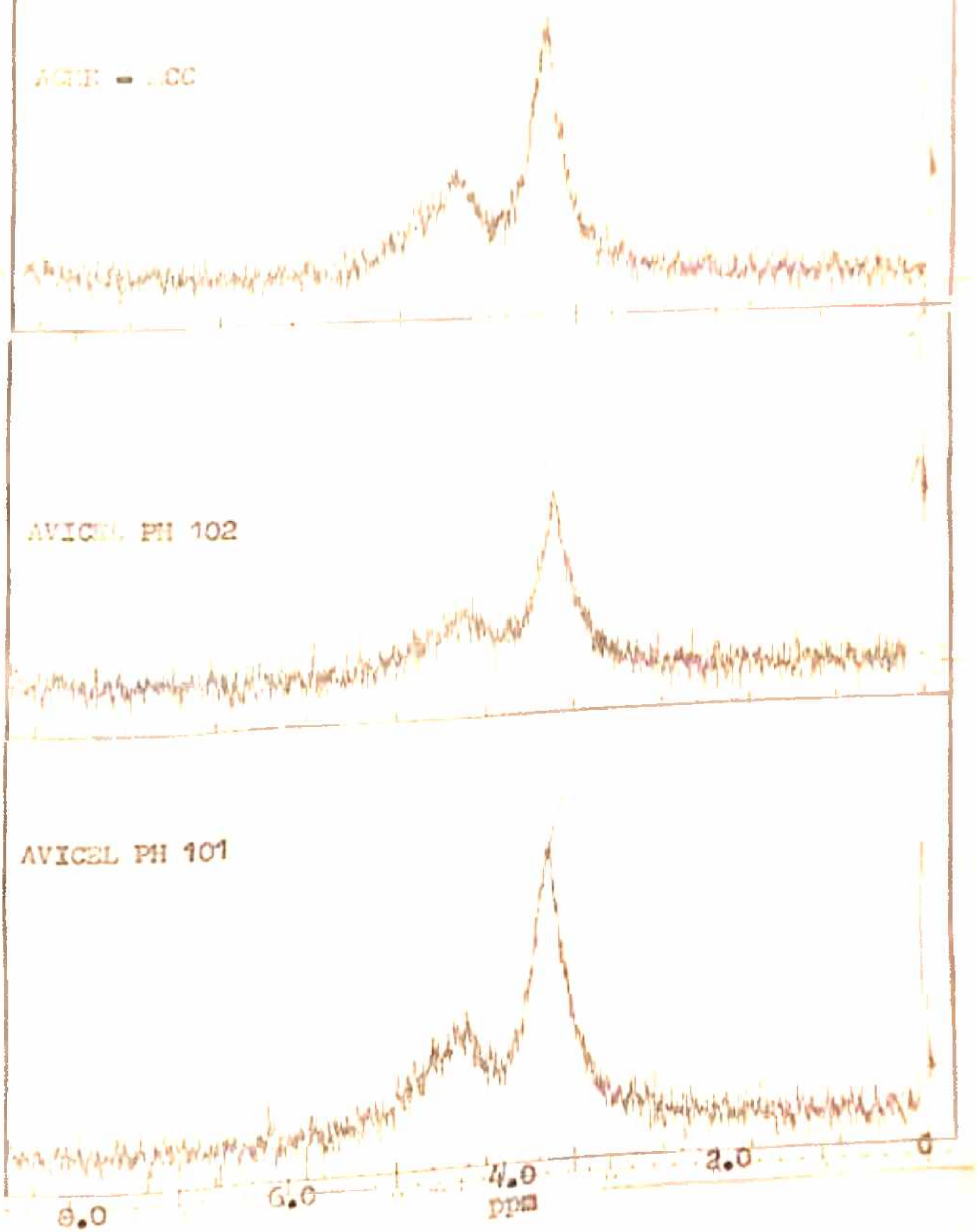
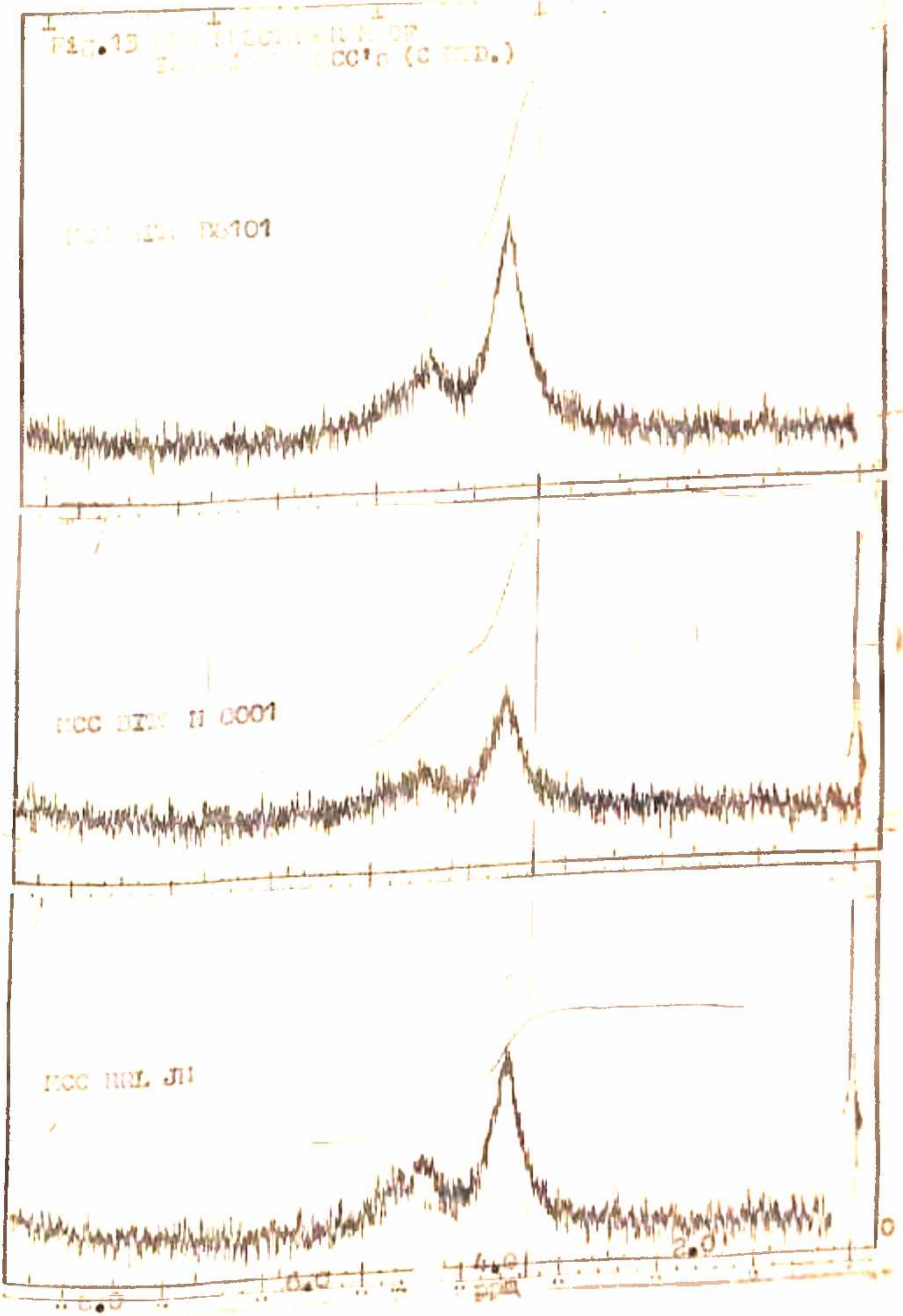


Fig.13 [illegible] OF
[illegible] CC'n (CONTD.)



overlapped by TFA peaks. This differentiation may be possible if the analysis is done on a 400 MHz NMR, compared to the present 60 MHz NMR. But for comparison, as all the samples were giving super imposable NMR plots, it is certain that chemically and structurally they are similar and MCC's prepared from waste cellulose are comparable to marketed varieties.

e. Flame Photometry for Na, K and Ca content of MCC's

The use of flame photometry for Na, K and Ca estimation is well known (Gearien and Grabowski, 1969). To assess the levels of the contamination with the above ions standard and sample solutions were prepared as below, for the analysis.

Sodium Standard: Dissolved (0.2542 g) sodium chloride in 100 ml of deionized water (1000 ppm). Diluted the solution to get 2, 4, 6, 8 and 10 ppm.

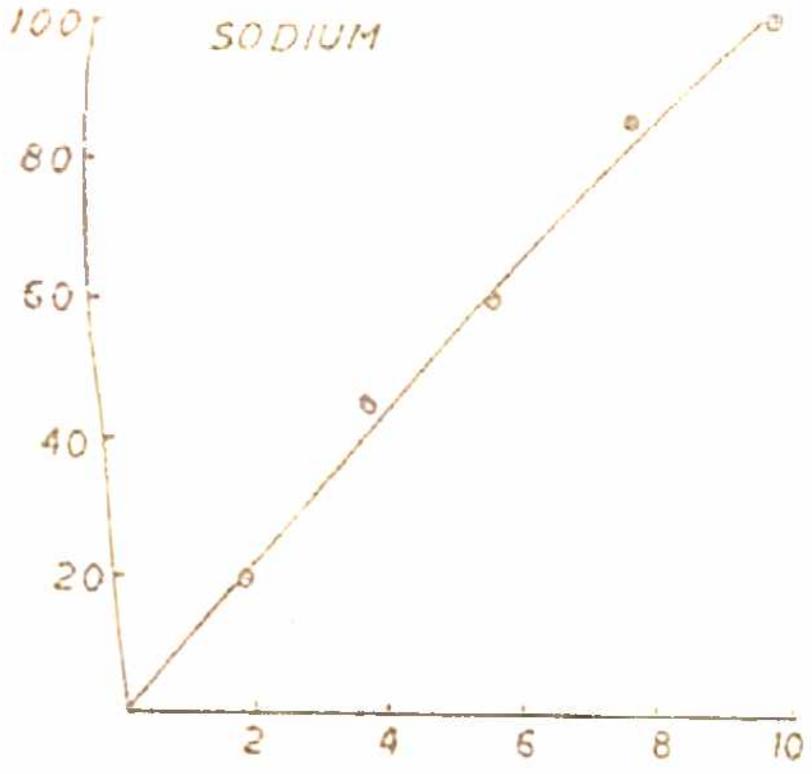
Potassium Standard: Dissolved (0.1907 g) KCl in (100 ml) deionized water (1000 ppm). Diluted to get 5, 10, 20 and 40 ppm.

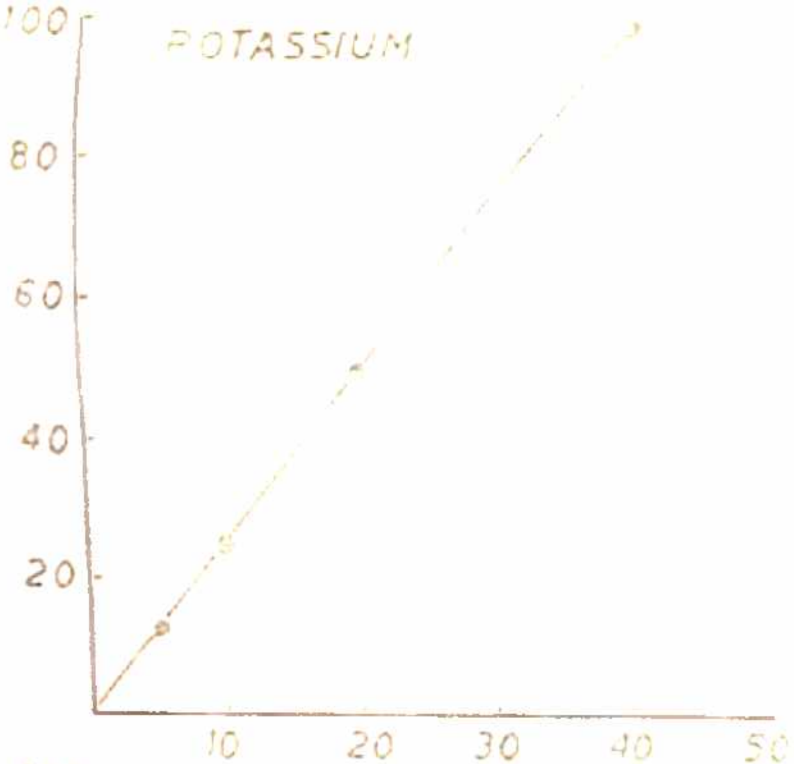
Calcium Standard: To calcium carbonate (1.249 g) in deionized water (50 ml) was added concentrated HCl (100 ml) dropwise to effect solution of $CaCO_3$. Made up the volume to 1 litre with deionized water (1000 ppm). Diluted the above solution to get 5, 10 , 20 and 25 ppm.

Sample Preparation: Microcrystalline cellulose (10g) accurately weighed was transferred to a clean platinum dish and ashed in an electric oven at 575 ± 25°, till the carbon was burnt away.

After cooling 6 N HCl (5 ml) was added and evaporated to dryness on a waterbath. Further 5 mls of 6 N HCl were added and again evaporated to dryness on a water bath. Finally 6 N HCl (5 ml) was added and heating done on a water bath for 5 minutes. The solution was transferred to (100 ml) volumetric flask with deionized water, diluted to volume and used for the analysis.

Elico flame photometer was used for the analysis. Various instrumental and analytical details and analysis of standard samples are given in Table 36. Concentrations of Na, K and Ca in various samples of MCC are given in Table 37. Standard plots for Na, K and Ca are in Figure 14.





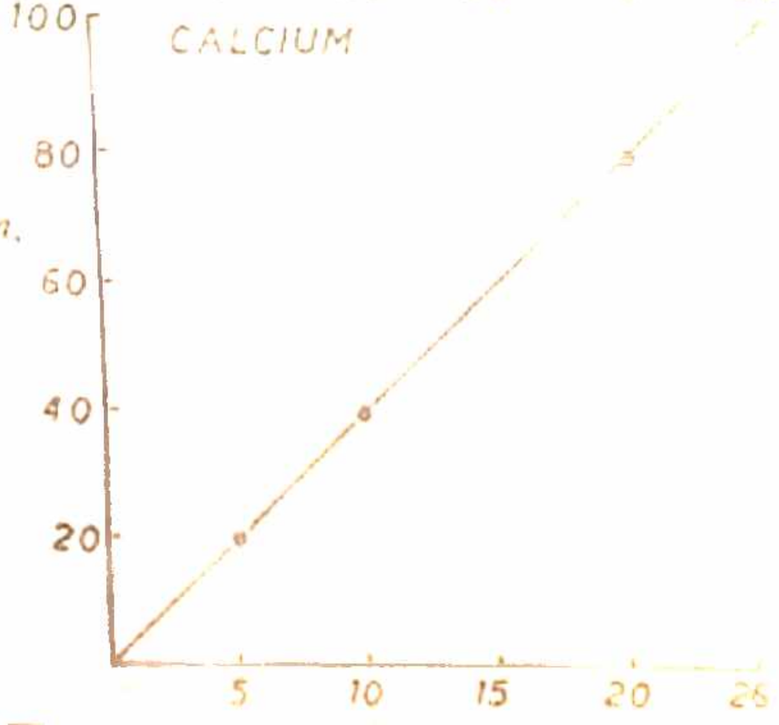


FIG.14. STANDARD PLOTS.
FLAME PHOTOMETRY.

ALL CONCENTRATIONS IN ppm.

TABLE - 36

Instrumental and analytical details, and, standards for Na, K and Ca analysis by flame photometry

Sl No	Details	Sodium		Potassium		Calcium	
1	Instrument	Flame photometer					
2	Mode	emission		emission		emission	
3	Wave length, nm	589		766		425	
4	Flame-gas	A-Ac		A-Ac		A-Ac	
5	Light source	Self		Self		Self	
6	Sensitivity check	Std.plot		Std.plot		Std.plot	
7	Standard samples	NaCl		KCl		$CaCO_3$	
8.	Standard readings	Conc ppm	% Reading	Conc. ppm	% Reading	Conc. ppm	% Reading
		2	20	5	12.5	5	20
		4	45	10	25	10	40
		6	60	20	50	20	80
		8	85	40	100	25	100
		10	100				

A-Ac- Air-Acetylene

TABLE - 37

Na, K and Ca Content of Various MCC's

Sl No.	Sample	Na	K	Ca
1	Avicel PH 101	0.1	Not more than 0.2	B.D.L.
2	Avicel RC 591	0.1	"	2.4
3	Avicel CL 611	0.1	"	2.4
4	Acme-MCC	BDL	"	4.0
5	MCC-RRL	1.6	"	4.0
6	MCC BITS N 8001	1.7	"	2.2
7	MCC BITS B 8101	3.7	"	2.2
8	MCC BITS N 8132	0.7	"	2.4

BDL - Below Detection Level

Sodium content of MCC's prepared from cellulosic wastes was comparable to marketed varieties. MCC-Acme and MCC-RRL showed highest level of sodium (4 mg/g each) and MCC's prepared from newsprint and bagasse showed lowest (2.2 mg/g each). Sodium content of Avicel PH 101 was below detection limit (BDL). Potassium content was below 0.2 mg/g for all the samples of MCC. Calcium content was maximum in MCC-BITS B 8101 (3.7 mg/g) and minimum in all the samples of avicel (0.1 mg/g). MCC-Acme showed calcium content below detection level. The reason for high content of calcium in MCC-bagasse (3.7 mg/g) was not known.

f. Atomic Absorption Spectroscopy (AAS) for Zn, Cu, Mn and Pb analysis

Analysis of Zn, Cu, Mn and Pb by AAS is well known. (Christian and Feldman, 1970). Standard samples of Zn (1ppm) Cu (5 ppm) and Mn (2 ppm) were prepared. MCC were prepared as mentioned in flame photometry sections. Perkin-Elmer 207 AAS was used for the study. For Pb analysis standard solutions were prepared by dissolving lead nitrate $Pb(NO_3)_2$. 0.1598 g in (100 ml) 1% HNO_3 (1000 ppm). Diluted the solution to make 2, 4, 6, 8 and 10 ppm. Sample preparation was made by dissolving MCC (50 mg) accurately weighed in a small amount (5 ml) of 72% H_2SO_4. Diluted to volume with 1% HNO_3 and used the clear solution for direct aspiration. Pb analysis was made on Instrumentation Laboratory aa/ae spectrophotometer

(RRL, Jammu) with aspiration rate of 5-6 ml/min at 16 psig. Instrumental and analytical details, and, concentration of Zn, Cu and Mn in various MCC samples are given in Table 38. Lead standard and sample analysis are in Table 35.

TABLE - 38

Zn, Cu, and Mn analysis by AAS- Instrumental and analytical details, Standards and content in various MCC's

Sl No.	Details	Zn	Cu	Mn	Pb
1.	Mode	abs	abs	abs	abs
2.	Wave length, nm	214	325	280	217
3.	SBW^{b}, nm	0.7	0.7	0.2	0.5
4.	Flame gas	A-Ac^{c}	A-Ac	A-Ac	A-Ac
5.	Light source	HCL^{d}	HCL	HCL	HCL
6.	Sensitivity check ppm	1.0	5.0	2.0	2-10
7.	Standard sample, metal	Zn	Cu	Mn	$Pb(NO_3)_2$
8.	Error in reading ±%	2	2	5	2
9.	Sample conc^{n}, ppm				
	Avicel PH 101	58	4.4	BDL^{e}	
	Avicel RC 591	82	2.8	"	
	Avicel CL 611	18	1.2	"	
	Acme-MCC	22	3.2	1.8	
	MCC-RRL	66	6.2	2.2	
	MCC BITS N 8001	128	44.0	3.6	
	MCC BITS B 8101	140	36.4	3.2	
	MCC BITS N 8132	54	22.2	2.6	

abs - absorption

SBW^{b} - Slit Band Width

A-Ac^{c} - Air- Acetylene

HCL^{d} - Hollow Cathode Lamp

BDL^{e} - Below Detection Limit

TABLE - 39

Lead analysis by AAS - Standards and Samples of MCC'S

Lead			MCC	
Sl No	Standards Conc,ppm	Abs	Samples	Pb, ppm
1	2	0.010	Avicel PH 101	9
2	4	0.017	Avicel PH 102	4
3	6	0.024	Acme-MCC	10
4	8	0.030	MCC RRL	2
5	10	0.038	MCC BITS N 8001	4
6			MCC BITS B 8101	3

Zinc content (Table 38) was maximum in MCC BITS B 8101 (140 ppm) and minimum in Avicel CL 611 (18 ppm). Though the Zn content of various MCC's was comparable, bagasse and newsprint MCC (N 8001) contained very high amounts. It may be due to external contamination of the two batches. Copper was in maximum in MCC-BITS N 8001 (44 ppm) and minimum in Avicel CL 611 (1.2 ppm) and was unusually high in MCC's prepared from cellulosic wastes. Exact reason was not known. It may be due to external contamination. Mn was below detection limit in all samples of avicel. It was maximum in newsprint MCC (3.6 ppm). Pb content was comparable in all the samples analysed (Table 39). It was maximum in Acme MCC (10 ppm) and minimum in MCC-RRL (2 ppm).

8. Differential Thermal Analysis of MCC'S

Pyrolytic degradation of cellulose has been well investigated (Shafizadeh, 1968). Cellulose degradation, goes through a gradual degradation,

TABLE - 39

Lead analysis by AAS - Standards and Samples of MCC'S

Lead			MCC	
Sl No	Standards Conc,ppm	Abs	Samples	Pb, ppm
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8. Differential Thermal Analysis of MCC'S

Pyrolytic degradation of cellulose has been well investigated (Shafizadeh, 1968). Cellulose degradation, goes through a gradual degradation, decomposition and charring at low temperature, and a rapid volatalization accompanied by formation of levoglucosan on pyrolysis at higher temperatures. Degradation reactions include depolymerization, hydrolysis, oxidation, dehydration and decarboxylation. Degradation is observed to be more in presence of oxygen and less in its absence (Major, 1958). Heating leads to carbonyl group formation ($>C=O$) as measured by IR Spectroscopy and standard reducing tests for carbonyl groups (Higgins, 1958).

Differential Thermal Analysis (DTA) shows a dip at about 290° representing endothermic reaction. It reaches maxima between $320-360^\circ$ and a sudden sharp rise indicates exothermic reaction which extends upto $350-380^\circ$. Thermo Gravimetric Analysis (TGA) in the same thermogram, shows rapid loss in weight during endo and exothermic reactions leaving behind a small amount of charred residue. During the reaction, cellulose follows through a concurrent and complex mechanism leading to C-O and C-C bond breaking and forming H_2O, CO_2, CO and C.

DTA of MCC's was undertaken to study the thermograms of different samples, to compare them with cellulose thermograms and to assess impurities and chemical nature of celluloses.

MCC (100-120 mg) accurately weighed was mixed with about 200 mg of alumina in a platinum crucible. The sample was heated from room temperature to 500° at the rate of 10°/min, in presence of oxygen in a Derivatograph MOM-OD 103, for thermal analysis studies. Figures 15-17 give thermograms of Avicel PH 101, Avicel PH 102 and MCC BITS N 8001. A sharp

Fig. 16
Thermogram of
Avicel PH 102

Wt. of samples-120 mg
Sensitivity -200 mg
Heating rate -5°/10° per min

Fig.17
Thermogram of
[illegible]

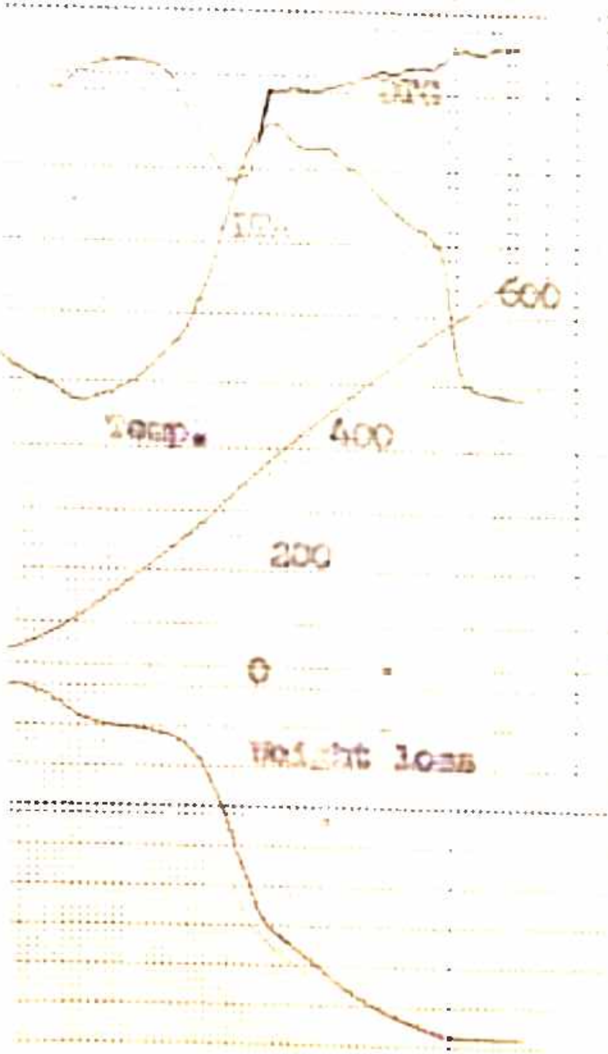
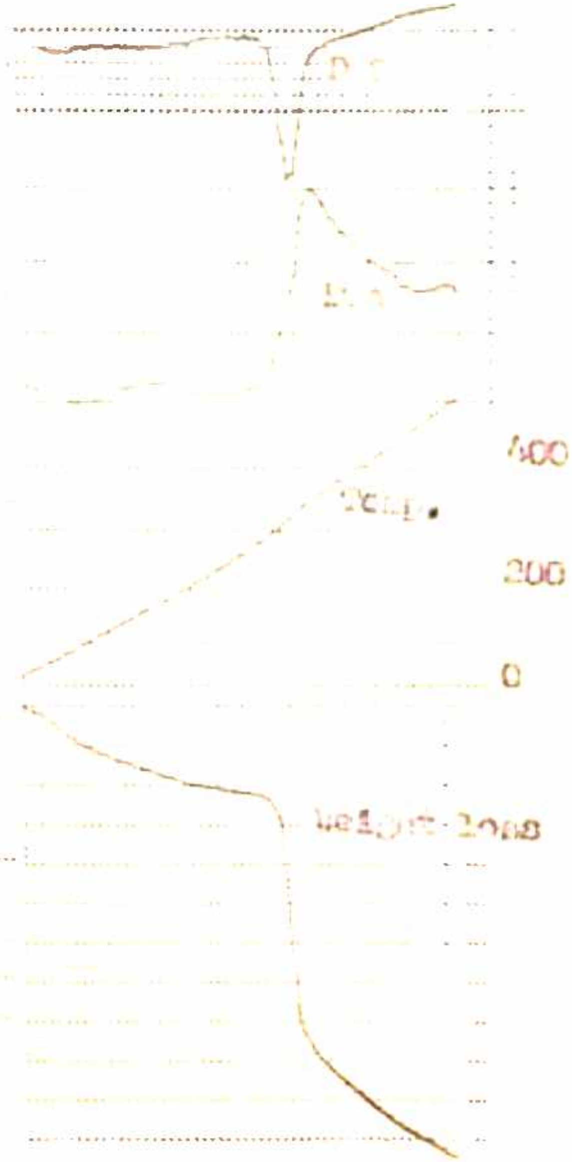


Fig.15
Thermogram of
Avicel PH 101



dip occured at 320° for Avicel PH 102 and MCC-BITS N 8001 and at 360° for Avicel PH 101. Cotton cellulose gives a sharp dip at 364° and cellulose acetate between 374-382°.

Thermograms of the 3 samples of MCC were comparable and in case of Newsprint MCC the dip was slightly broad.

h. Optical and Electron Microscopy

Electron micrographs were taken on Jeol JSM-35, with scanning mode and optical micrographs were taken on Carl-Zeiss (Zena) microscope with camera attachment facility. The Micrographs were taken to access the shape, size and surface texture of MCC's (Figure 10.1-10.13). All the samples showed rod shaped crystals of varying sizes, single as well as aggregates joined like match sticks. In case of Avicel RC 591, Avicel CL 611, which contain 12-16% Carboxyl methyl cellulose (CMC) with MCC, round shaped crystals are observed. This is because CMC forms a coat on MCC which when suspended in glycerol (optical microscopy) swells and gives round and not rod shape crystals.

Optical and electron micrographs of MCC's prepared from cellulosic wastes were comparable to standard varieties.

All the important characteristics of MCC's studied in the present work have been summarized for easy comparison and evaluation.

Fig.18.1 AVICEL PH 101 x 200

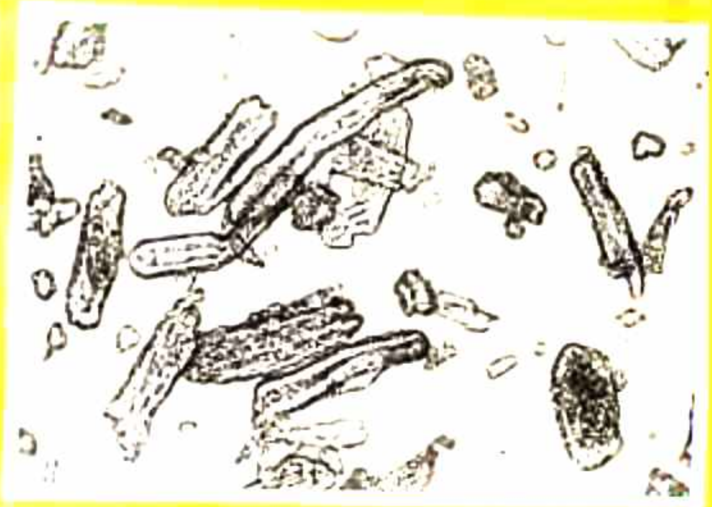


Fig.18.2 AVICEL PH 102 x 200

Fig.18.3 AVICEL CL 611 x 200

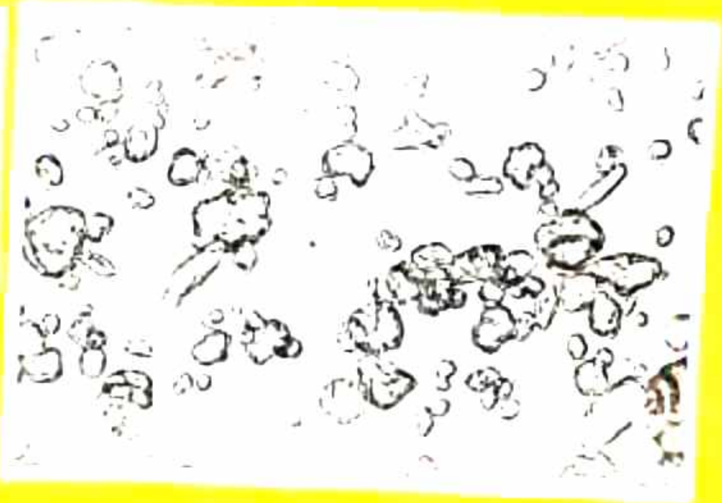


Fig. 18.4 AVICEL RC 591 x 400

99f

Fig.18.5 MCC-LGBA x 200

Fig.18.1 OPTICAL MICROGRAPHS OF MCC
-18.10

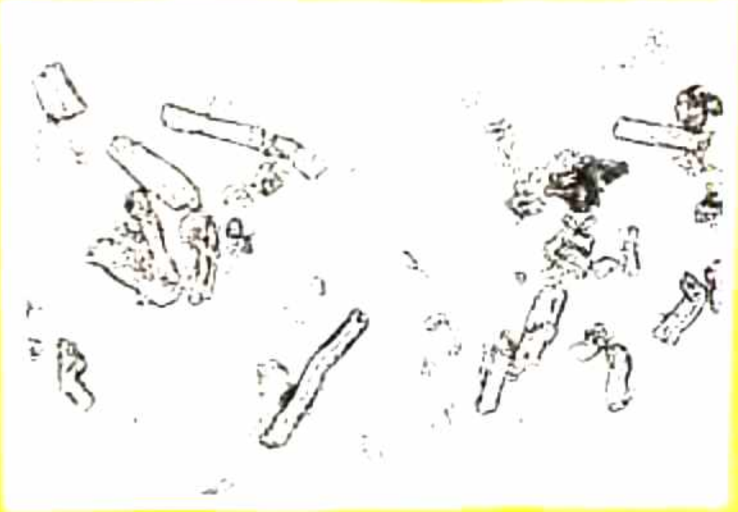


Fig.18.6 MCC - ACME x 200

Fig.18.7 MCC - CPI x 200

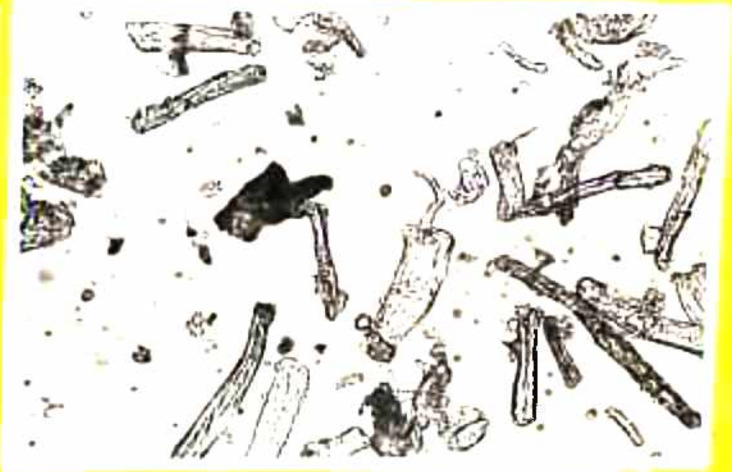


Fig.18.9 MCC BITS B 8101 x 200

Fig.18.8 MCC-BITS N 8001 x 200

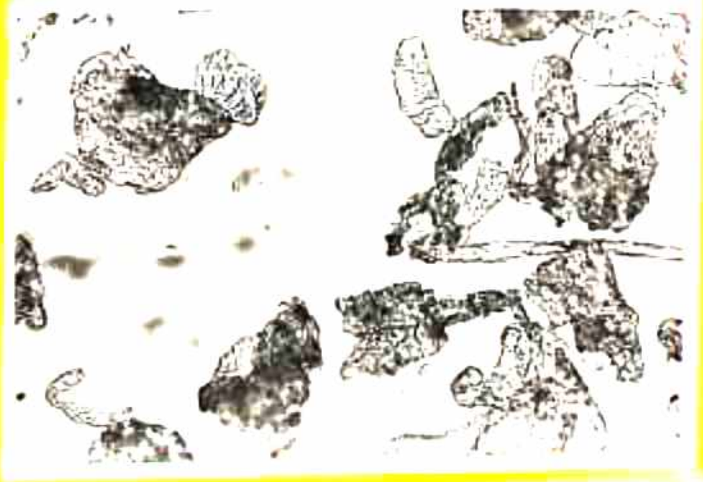


Fig.18.10 MCC-BITS C 8201 x 200

Fig.18.11 AVICEL PH 101 x 500

Fig.18.12 [illegible] - MCC x 500

Fig.18.13 MCC- RRL x 500

Fig.18.11 ELECTRON MICROGRAPHS OF MCC
-18.13

TABLE - 40

IMPORTANT CHARACTERISTICS OF MCC's

Sl No.	MCC	Particle size, µ	DP	Mol.wt.	pH of 12.5% dispersion	Loss on drying 105°	X-ray diffraction crystallinity %	IR crystallinity %	DRS whiteness %	Bulk density A gm/cc	Bulk density P gm/cc	Angle of repose °	Zn,Cu Mn & Pb by AAS	Na,K & Ca by FP	Cl,SO$_4$ & AS limits	Micrographs
1-	Avicel PH 101	13	350	56,720	6.0	Not more than 3%	83.57	66.67	92	0.27	0.37	45	Comparable to standards		Within Pharmacoepial limits	Rod shaped crystals, single as well as aggregates
2	Avicel PH 102	25	143	23,200	7.0		85.46	88.88	91	0.38	0.50	48				
3	Avicel CL 611	35	195	31,520	6.8		85.00	60.00	90	0.30	0.48	47				
4	Acme-MCC	9	207	33,600	6.8		84.25	66.67	86	0.38	0.59	52				
5	MCC-RRL	15	143	23,200	6.7		84.24	75.00	89	0.32	0.50	45				
6	MCC-CPI	25	244	39.520	6.8		81.25	72.22	83	0.28	0.40	48				
7	MCC BITS N 8001	14	275	44,200	6.4		81.20	57.19	65	0.25	0.37	48				
8	MCC BITS B 8101	11.4	136	22,032	6.6		82.86	69.23	81	0.28	0.42	46				
9	MCC BITS C 8201	20	234	37,908	6.4		83.56	71.43	71	0.30	0.50	47				
10	Hydrocellulose	30	219	35,520	6.8		84.35	92.59	79 98(MgO-Std)	0.27	0.45	50				
11	MCC-BPC	10-50	222	36,000												

IRS - Infrared Spectroscopy
AAS - Atomic Absorption Spectroscopy
FP - Flame Photometry

DRS - Diffuse Reflectance Spectroscopy
A - Aerated
P - Packed

CHAPTER - VI

Utility of MCC in Solid Dosage Forms

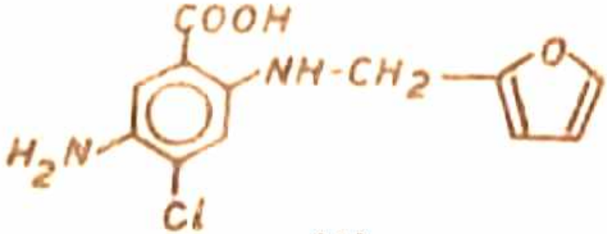
MCC is extensively used in solid dosage forms such as tablets, capsules etc. It is an inert diluent, disintegrant and lubricant. Literature (Chapter-I) gives extensive research carried out on MCC as an additive in solid dosage forms. The aim of the present exercise was to study the potential of MCC prepared from cellulosic wastes as an additive in solid dosage forms.

Frusemide (diuretic) tablets were prepared by mixing the drug with MCC obtained from bagasse and corncob wastes and the tablets were compared with the marketed tablets of the same drug (DIURAL, Alembic) for drug content, weight variation, hardness, friability, disintegration time, physical dimensions and defects.

RLX hydrochloride (bronchodilator) capsules were also prepared by mixing the drug with MCC and filling in capsules. RLX-HCl is a potent bronchodilator, prepared by RRL, Jammu, which is about 10 times potent, when compared to aminophylline.

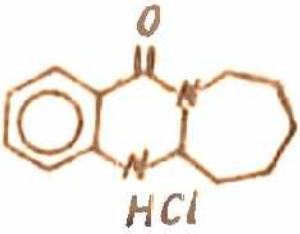
Structures of frusemide and RLX-HCl are in Fig.20 and their λ_{max} in 0.1N NaOH and distilled water are in Fig.21

FIG. 20. STRUCTURE OF FRUSEMIDE (A) AND RLX-HCl (B)



(A)

4-CHLORO, N-FURFURYL, 5-SULFAMOYL, ANTHRANILIC ACID.



(B)

5-PENTA HYDRO, TROPYLIUM, QUINAZOLINE, 11-ONE, HYDROCHLORIDE.

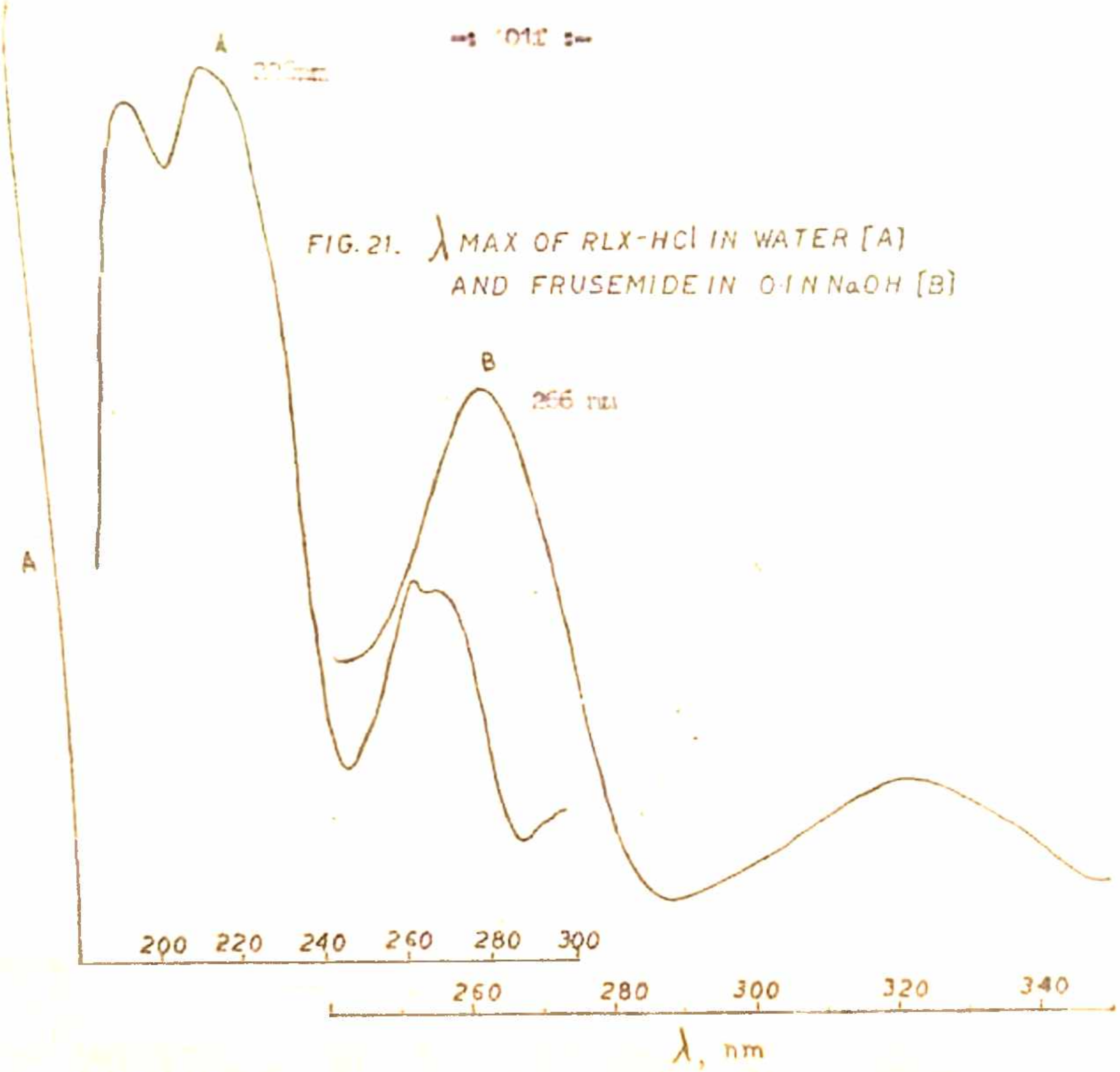


FIG. 21. λ MAX OF RLX-HCl IN WATER [A] AND FRUSEMIDE IN 0·1 N NaOH [B]

Formulation of Frusemide tablets

Frusemide powder (2g) was mixed with MCC (7.5 g). Tablets were punched after mixing 2% talc as lubricant, on a single punch, hand operated tableting machine. Amount of frusemide per tablet was 40 mg and 50 tablets were punched for each set. Tablets so prepared were compared with marketed frusemide tablets (Diural, Alemtic) for drug content, weight variation, physical defects, disintegration time, hardness and friability. Results are in table 41.

Drug content: Frusemide tablets (5) were powdered in a pestle and mortar, triturated with 0.1 N NaOH and diluted to (50 ml) volume with 0.1 N NaOH. Filtered and diluted the filtrate (2.5 ml) to (50 ml) volume with 0.1 N NaOH solution. Read absorbance at 270 nm with 1.0 cm cell on Hitachi Perkin-Elmer 139 Spectrophotometer. A standard plot of frusemide, varying concentrations vs Absorbance was made (Fig.22).

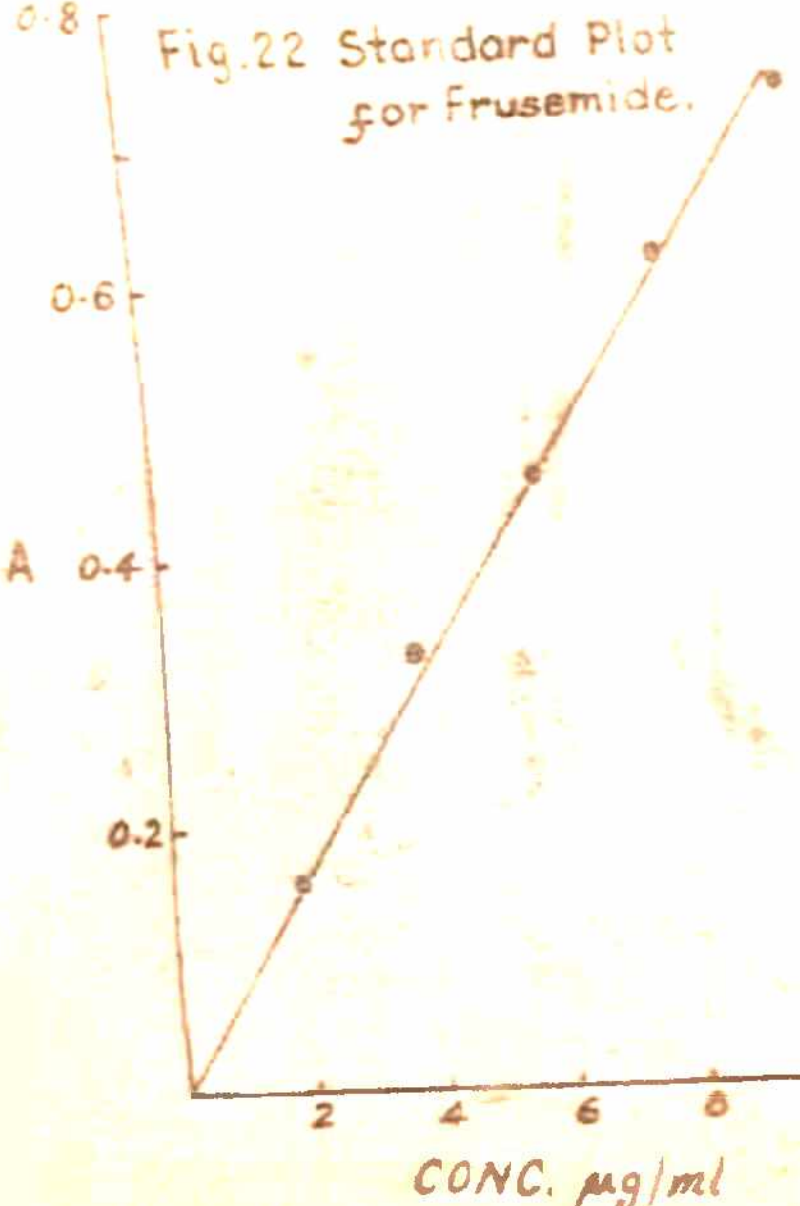


Fig.22 Standard Plot for Frusemide.

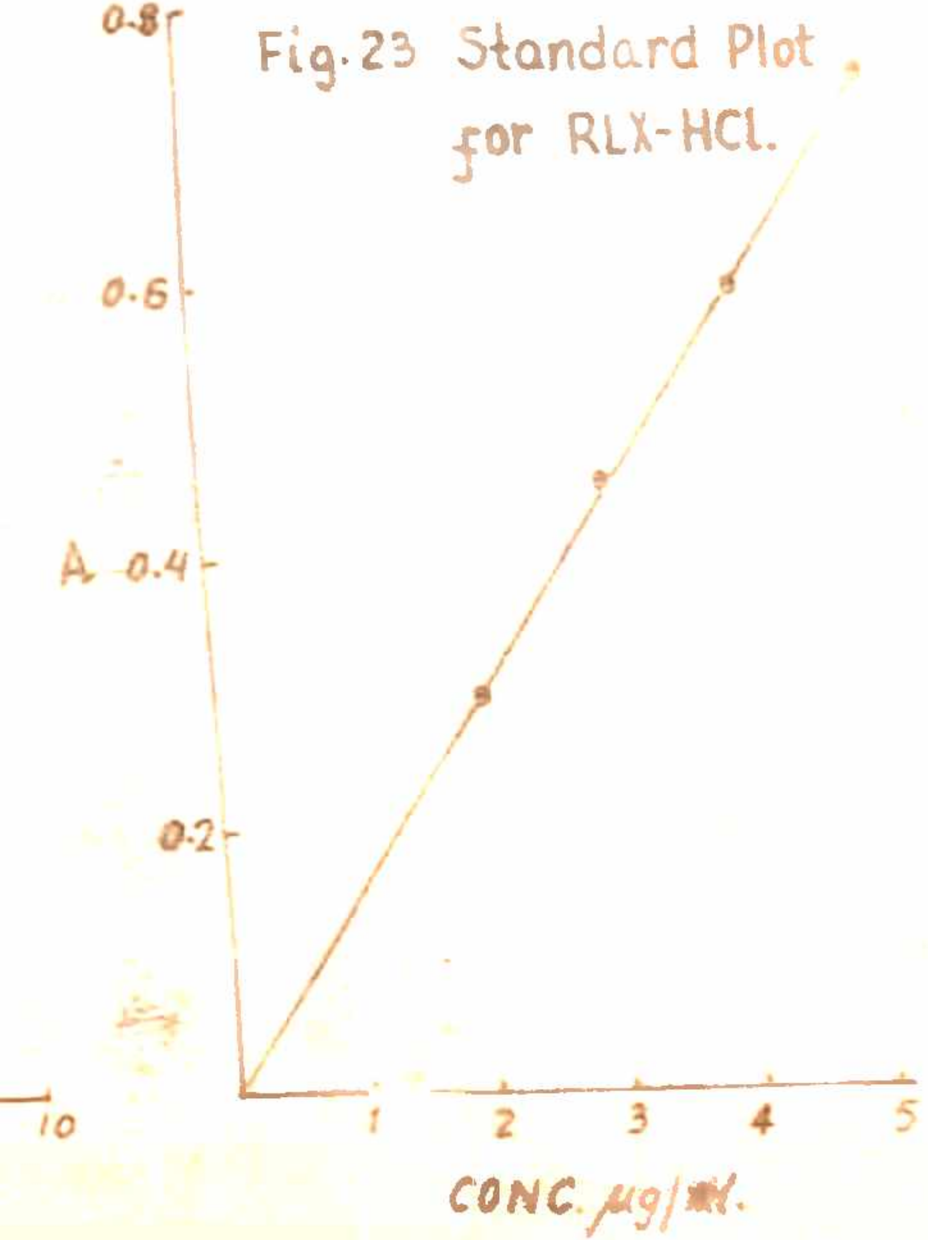


Fig. 23 Standard Plot for RLX-HCl.

TABLE - 41

Analysis of Frusemide Tablets

Frusemide per tablet - 40 mg

Tablet Analysis	DIURAL	Frusemide Tablets Corncob MCC	Bagasse MCC
1 Drug content mg/tab	41.60	38.00	38.20
2 Weight variation average wt, mg	176-212 193	125-152 139	150 - 190 165
3 Hardness kg/cm^2	~~193~~ 5.0	~~139~~ 5.0	~~165~~ 4.0
4 Friability, %	1.70	1.30	3.70
5 Disintegration time, min.	2	3	2
6 Thickness, mm diameter, mm	3.0 8.0	2.0 10.0	2.5 10.0
7 Physical defects	Nil	Nil	Collaring picking

Formulation of RLX HCl Capsules

RLX HCl (2.5 g) was mixed with MCC (2.5 g) and filled in capsules on a hand filling capsule holder. Amount of RLX HCl per capsule was 50 mg and 50 capsules were prepared. Capsules were analysed for drug content, weight variation and disintegration time, from time to time. Results are in Table 42.

TABLE - 42

Analysis of RLX HCl capsules:Amount of RLX HCl per capsule - 50 mg

Sl No	MCC Type Annlysis	Avicel PH 102	MCC RRL	MCC BITS N 8001	MCC BITS B 8101	MCC BITS C 8201	Avicel PH 101
1	Drug content, mg/caps	49.56	52.50	48.00	46.60	48.30	46.60
2	Disintegration time, min	Less than 20					
3	Weight variation mg	155 to 171	155 to 174	158 to 179	154 to 171	154 to 172	155 to 175
	average weight mg	160	162	161	159	159	162

Drug content: The contents of a capsule were transferred to a (50 ml) volumetric flask with the aid of distilled water and absorbance was read at 226 nm on Pye-Unicam Spectrophotometer using 1 cm cells. A standard plot of absorbance vs concentration of RLX-HCl in distilled water was made (Fig.23). Drug content was analysed immediately after formulation and every month for a period of 6 months. Results are in Table 43.

TABLE-43

Drug content of RLX HCl capsules analysed every month for 6 months.

RLX HCl per capsule - 50 mg

Sl No	Duration days/ MCC Type	0	35	72	102	124	145
		Drug Conten					
1	Avicel PH 101	46.60	52.59	50.00	49.00	49.12	50.26
2	Avicel PH 102	49.56	49.10	50.00	49.90	47.37	51.14
3	Acme-MCC	46.00	47.40	54.50	50.00	47.98	51.75
4	MCC-RBL	52.50	50.80	50.14	51.60	52.28	54.91
5	MCC BITS N8001	48.00	49.83	49.11	46.60	46.50	46.50
6	MCC BITS B8101	46.60	48.30	48.82	46.60	50.80	51.75
7	MCC BITS C8201	48.30	53.45	50.64	49.06	51.75	49.75

Frusemide tablets prepared from corncob and bagasse MCC were satisfactory with respect to drug content, hardness and disintegration time, when compared to marketed Diural tablets. Bagasse-MCC tablets showed higher friability when compared to the other two types of tablets, apart from showing collaring and picking on the tablets. Friability could be reduced by increasing the hardness from 4 kg/cm^2 to 5 kg/cm^2 and, picking could be overcome by either increasing the amount of MCC added or by mixing a small amount of talc as lubricant. Collaring was due to worn out die and punch.

RLX-HCl capsules prepared from standard MCC and MCC prepared from cellulosic wastes were comparable. After 6 months of formulation drug was found intact in the capsules along with MCC.

Hence, MCC prepared from cellulosic wastes such as newsprint, bagasse and corncob could be used as an economic additive in solid dosage forms.

CHAPTER VII

SUMMARY AND CONCLUSIONS

The present thesis deals with the recycling of cellulosic wastes into commercially important MCC. The aim was to evolve an economical method for conversion of corncob, bagasse and newsprint into good quality MCC comparable to marketed varieties. Another objective was to isolate by-products such as furfural and sugars.

Cellulosic wastes were analysed proximately for the percentage of cellulose, lignin and pentosans, following TAPPI (1968) methods. Absorbent cotton, bagasse, corncob and newsprint had 95.8%, 63.8%, 81.5% and 61.0% holocellulose respectively. Pentosan content was same for bagasse and corncobs (29%) but newsprint had low pentosan content(17.3%). Newsprint had highest lignin (28%) amongst the above four materials followed by bagasse (22%) and corncob (11%). Pentosan and lignin contents of absorbent cotton were too low compared to other cellulosic materials. Corncob has minimum lignin as compared to other cellulosic wastes and could be handled easily for isolation of cellulose and its conversion into MCC.

MCC was prepared from corncob, bagasse and newsprint. The steps involved in the preparation of MCC from corncob and bagasse were prehydrolysis, multistage bleaching, hydrolysis and mechanical disintegration. In the case of newsprint the steps were deinking, multistage bleaching, hydrolysis and mechanical disintegration.

Prehydrolysis was done with 0.1% and 1.0% alkali separately at solid liquid ratios of 1:5, 1:6, 1:8 and 1:10 for 24 hours at room temperature and at 75°. The pulp was bleached by multistage (3 stages) bleaching with chlorine, chlorite and chlorine dioxide. Hydrolysis was carried out with HCl (0.5N-5.0N). 2.0 and 2.5N were found to be satisfactory. Bagasse prehydrolysis was done at 130°, 25 psi for 2 hours with 10-120% sodium hydroxide (based on bagasse). Autoclaving time of 1.5 hours with alkali concentrations of 40% (based on bagasse) and four stage bleaching gave satisfactory results.

Hydrolysis could be carried out with H_2SO_4 as it is easy to separate it from other products. During hydrolysis amorphous region gets knocked off leaving behind acid resistant crystalline chains.

Newsprint was deinked with surf powder which compared well with synthetic surfactant like Sodium Lauryl Sulphate (SLS). Six stage bleaching (CECEDP) was satisfactory. Hydrolysis was done with 2.5N HCl.

Gamma irradiation depolymerises cellulose. Doses between 8.5-12 Mrad gave DP of 200-300. Gamma irradiated cellulose on hydrolysis with HCl(1.5 N-2.0 N) and mechanical disintegration gave MCC. Gamma irradiation increases sugar content, copper number and alkali solubility of cellulose due to the formation of new carbonyl groups and lower DP chains. Levelling-off observed in acid hydrolysis is not seen in gamma radiolysis, because of high penetrating power of gamma rays.

Gamma irradiation also makes cellulose susceptible to acid and enzymatic hydrolysis.

The $\overline{DP}$ of Avicel pH 101 was found to have the maximum $\overline{DP}$ of 350 and MCC BITS B0101 showed minimum $\overline{DP}$ (136) and rest of the samples had values between these two values. MCC prepared from bagasse showed lowest particle size (11 microns) and Avicel CL 611 had the highest particle size (35 microns). Hydrocellulose also had a particle size of 35 microns. Chloride, sulphate and arsenic were within pharmacopoeial limits. Properties like bulk density, and angle of repose of standard and prepared MCC's were comparable.

X-ray diffraction (XRD) crystallinity of Avicel pH 102 was highest (85.5%) and that of MCC prepared from newsprint waste was the lowest (81.2%). The reflections in XRD were due to the following planes - 101, $10\bar{1}$, 002 and 103 of which 002 plane reflection was the strongest in all the cases. All MCC samples had comparable hkl values (Miller indices). Infrared crystallinity of hydrocellulose was the highest (92.6%) and that of MCC prepared from newsprint waste the lowest (57.1%). Diffuse Reflectance Spectroscopy (DRS) showed whiteness above 60% for all the samples with Avicel pH 101 showing highest (92%) and MCC BITS N8001 the lowest (65%) in comparison to MgO (98%) reference standard.

All the MCC samples showed superimposable NMR. Sodium content of MCC samples varied from 2.2 mg/g to 4.0 mg/g and potassium was below 0.2 mg/g for all the samples. Calcium content

was more in MCC-BITS B0101 (3.7 mg/g) and less in Avicels (0.1 mg/g) and in Acme-MCC it was below detection limit. Zinc was maximum in MCC-BITS B8101 (140 ppm) and minimum in Avicel CL611 (18 ppm). Copper was maximum in MCC BITS N 8001 (44 ppm) and minimum in Avicel CL611 (1.2 ppm). Manganese was below detection limit in all the samples of Avicel and it was maximum in MCC BITS N8001 (3.6 ppm). Lead content was comparable in all the samples, Acme-MCC showing the highest (10 ppm) and MCC-RRL the lowest (2 ppm). DTA of MCC's analysed showed a dip between 290-360° for endothermic reaction followed by a sharp rise indicating the exothermic reaction.

In optical and electron microscope all the MCC samples showed rod shaped single or aggregated crystals of varying sizes. In case of Avicel CL611 and Avicel RC591 round crystals are seen, because, MCC is coated with CMC in these samples and they swell in presence of solvent.

Frusemide tablets and RLX. HCl capsules prepared with MCC from cellulosic wastes gave satisfactory results when analysed for their qualities. Drug was found stable after 6 months in RLX HCl capsules.

Lignin, furfuraldehyde and sugars can be recovered in the production of MCC from cellulosic wastes. The production does not involve sophisticated equipments and skilled personnel and hence, cottage units can be set up for recycling of cellulosic wastes into MCC.

Future Trends in MCC Research

The past and present research on MCC, has opened-up new domains for further investigations.

How the atoms lie in the molecule, the molecules in the unit cell, the unitcells in the crystallite, the crystallites in the microfibril, the microfibrils in the cellulose fibre? Where and how are the crystalline and amorphous regions located? How do they differ in their structures? Some interesting work is done in the above areas, but, only surface has been scratched and as such intensive research is possible to unfold answers to these querries.

MCC can be chemically modified to eliminate existing deficiencies. Topochemical derivatisation of MCC with a controlled degree of substitution to produce Microcrystalline-Carboxy Methyl Cellulose (MC-CMC) can give a product having qualities of CMC as well as MCC. MC-CMC combination can be a better tablet disintegrant and suspending agent compared to MCC or CMC alone. Similarly spherodization of MCC to get free flowing spheres of appropriate diameter can give better flow properties compared to the parent MCC. Incorporating drugs within the micelles of MCC to improve their stability and compatibility seems another promising area.

Some new applications of MCC could be tried. MCC may prove to be a potential plasma extender as the molecular weight, $\overline{DP}$ and viscosity of both is comparable. Use of MCC in microencapsulation, preparation of controlled drug delivery devices and coating could be other promising areas.

Last, but not the least, studies on synthesis of cellulose from D-glucose may throw light on the molecular structure of MCC and cellulose.

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