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Quantitative Estimation of Avicel Polymer and its Impact on Spray Pattern, Plume Geometry and Droplet Size in Nasal Spray Products

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Abstract

Throughout the world, the regulatory agencies like US FDA, MHRA, Health Canada recommend that during the development of generic products like Nasal sprays, Ophthalmic solutions, the inactive ingredients in the generic product formulation must be qualitatively (Q1) and quantitatively (Q2) similar to the reference listed drug product. This requires a careful deformulation/reverse engineering study of the reference listed drug product or innovator product for all the listed inactive ingredients. Avicel is one of the most important ingredients primarily used in various Nasal spray and ophthalmic suspension products as a suspending agent. It is a mixture of microcrystalline cellulose and carboxy methyl cellulose. The aim of this study is to develop a simple yet robust analytical method for the accurate quantitative estimation of this polymer for generic product development to regulatory markets. We have not found any reported method for the accurate quantitation of this polymer from any of the pharmaceutical dosage forms. Hence, this article will certainly accelerate the generic development of different pharmaceutical dosage forms for regulatory markets.

Due to its non chromophoric nature, Avicel polymer is derivatized to a readily quantifiable compound by using diphenylamine reagent. The complex is measured at wavelength 635 nm without any interference. The polymer can be successfully quantified at concentration of 0.26 µg/ml and above from various pharmaceutical products such as tablets, nasal spray suspensions, ophthalmic products etc. This paper gives a simple yet accurate and precise method for the quantitative estimation of Avicel by derivatized spectrophotometry from various pharmaceutical products.

Keywords: Avicel; Quantitative estimation; Spectrophotometry; Derivatization; Diphenylamine; Spray pattern; Plume geometry

Abbreviations: US: United State; BP: British Pharmacopeia; FDA: Food and Drug Administration; ANDA: Abbreviated New; Drug Application; RLD: Reference Listed Drug; ICH: International Conference on Harmonization; MCC: Microcrystalline Cellulose; CMC: Sodium Carboxy Methyl Cellulose; NIR: Near Infra-Red Spectroscopy; LOD: Limit of Detection; LOQ: Limit of quantitation; SD: Standard Deviation; RSD: Relative Standard Deviation; FD: Forced Degradation; H: Hour

Introduction

Excipients are inactive ingredients of any finished pharmaceutical products. They provide stability to the active pharmaceutical ingredients (API). The different excipients include diluents or fillers, binders, disintegrants, lubricants, colouring agents and preservatives. Sometimes these excipients help in improving the biopharmaceutical profile, appearance and patient acceptability of finished pharmaceutical products. The use of right quality, type of excipient and accurate quantity is most important during the development of any medicinal product. The International guidelines like ICH, FDA gives more stress on the quality of such excipients. One of the most common excipient in oral solid dosage forms is Micro crystalline cellulose (MCC). It was discovered by Battista and Smith in 1955. It was later commercialized under the brand name Avicel®

Avicel (Figure 1) is used as a binder/diluent, anti-adherent and as disintegrant in various pharmaceutical products. It is a mixture of MCC and sodium carboxy methyl cellulose (CMC). MCC is partially depolymerized cellulose and is composed of

crystalline and amorphous domains [1]. MCC is prepared by the acid hydrolysis of cellulose [2]. The degree of crystallinity in MCC greatly affects its compactibility, flowability and the stability of the medicinal product [3]. During the manufacturing of MCC both softwoods and hardwoods are used as a possible source [4]. The moisture content, particle shape and particle size distribution varies among different grades of MCC samples. This makes a significant difference in the stability of pharmaceutical products. The low cost MCC grades are manufactured from various agricultural residues [5], sugarcane peel, bagasse [6,7], banana pseudo stem [8], groundnut shell [9], from cotton [10], corn husk [11] etc.

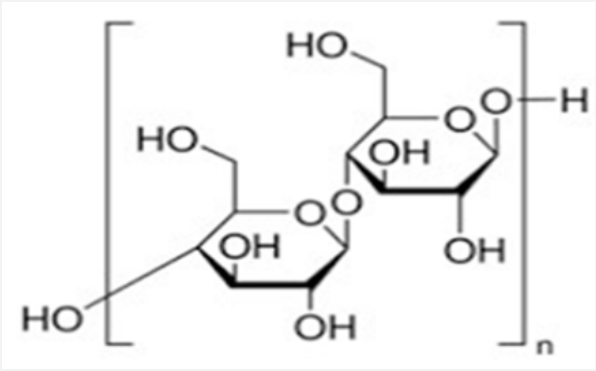

Figure 1: Chemical structure of Avicel pH.

Avicel® PH 101 (CAS No.9004-34-6) is commercial brand of MCC that is obtained from costly hard wood. Various grades of Avicel eg. RC-591, CL-611, RC 591F are currently being used in the pharmaceutical industry as excipients. The different grades of Avicel mostly differ in the percent composition of MCC and sodium CMC having different viscosity and pH.

There are stringent regulatory standards issued for nasal dosage forms in USA [12] and in Europe [13] which recommends that the inactive ingredients in the test product formulation be qualitatively (Q1) the same and quantitatively (Q2) essentially the same to the reference listed drug product. Hence, estimation methods for excipients appear crucial since any variation in excipients quantity would have a potential impact on the quality and stability of the developed pharmaceutical formulation [14].

For the pure excipients, the method used for the quantitative estimation by both European Pharmacopoeia and US Pharmacopoeia for Avicel [15,16] is by using the potentiometric titration method. This method cannot be used for the finished pharmaceutical products because of the interference from other excipients. Size exclusion chromatography with refractive index detector are used, however, because of the polymeric nature of the compound, the peak observed is not a sharp gaussian shape peak, because of which accurate quantitation is not possible. In one of the reported methods [17], the total cellulose content (MCC and CMC) of liquid formulations like nasal spray products is calculated by gravimetric method by determining the water content by evaporating the liquid portion and weighing the total solid mass obtained. The cellulose content is then determined by subtracting the contents of all other ingredients (actives and excipients) from the total solid. This method lacks both the accuracy and reproducibility since it is an indirect method of estimation.

Since excipients such as MCC is crucial for any pharmaceutical drug stability as discussed above, having its extract concentration estimated is equally critical. From our extensive literature search, we found merely two papers that discuss about estimation methods for MCC. These include Near Infra-Red (NIR) chemometric method [18] and an estimation method that involves dialysis, cellulase hydrolysis, and a reducing sugar assay [19]. Since the NIR method lacks sensitivity and requires special instrumentation. The hydrolysis method described by Zhang et al. is laborious and not sensitive enough, we explored the possibility of looking into developing estimation method of MCC that will be sensitive, quantitative and specific too. In the present research paper, the methodology for the quantitation of Avicel from nasal spray suspension product is explained in detail.

Material and Methods

Chemicals and reagents

AR grade Acetic Acid, Diphenylamine, Hydrochloric Acid, Ortho-phosphoric Acid, Hydrochloric acid, Sodium hydroxide and Hydrogen peroxide were purchased from Merck Limited, Mumbai, India. Avicel pH RC 591 was purchased from FMC Corporation, Philadelphia, PA 19103.

Preparation of diphenylamine reagent

3.75 gm of diphenylamine was weighed accurately and transferred into 250 ml volumetric flask. 150 ml acetic acid was added and sonicated to dissolve it completely. Further 90ml of

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hydrochloric acid was added and mixed well by sonication. The reagent needs to be freshly prepared before use.

Standard preparation

About 20 mg of Avicel pH RC 591 working standard was weighed accurately in 250 ml volumetric flask, about 175 ml ortho-phosphoric acid was added, the mixture was heated on water bath at 90°C till it is completely dissolved. The flask was then removed and kept for cooling at room temperature. The volume was made up to the mark with water, mixed well by using the sonicator and cooled at room temperature. Further, 1 ml of standard stock solution was diluted to 25 ml in a volumetric flask and the volume was made up to the mark with diphenylamine reagent, mixed well and transferred about 15 ml solution into the test tube. Heat the test tube filled with solution in a liquid paraffin oil bath set at 105°C ± 2°C for 90 min. The test tube is then cooled to room temperature in ice bath for 10 min.

Blank preparation

1 ml of 70% ortho-phosphoric acid was transferred into a 25 ml volumetric flask and diluted to volume with the diphenylamine reagent. 15 ml solution is further transferred into the test tube. The test tube with the solution was heated in a liquid paraffin oil bath set at 105°C ± 2°C for 90 min. The test tube is then cooled to room temperature in ice bath for 10 min.

Sample preparation

The Nasal spray suspension equivalent to 20 mg of Avicel pH RC 591 was accurately weighed and transferred into a 250 ml volumetric flask. About 175 ml ortho-phosphoric acid was added and the flask was heated in water bath at 90°C till it dissolves completely. The flask was then cooled at room temperature and volume was made up to the mark with water, mixed well and allowed to cool at room temperature.

Placebo preparation

The placebo solution was prepared on the same line to sample solution except the addition of Avicel. The placebo solution was accurately weighed and transferred into a 250 ml volumetric flask. About 175 ml ortho -phosphoric acid was added and the flask was heated in water bath at 90°C. The flask was then cooled at room temperature and volume was made up to the mark with water, mixed well and allowed to cool at room temperature.

Sample preparation for commercial products

The samples of excipients like Avicel, Microcrystalline cellulose, Sodium CMC and pharmaceutical dosage forms like Ophthalmic suspension and Tablet are prepared as per the procedure mentioned under sample preparation for nasal spray suspension for the determination of Avicel content.

Instrument used

UV-Vis Spectrophotometer (Make: Shimadzu Corporation, Kyoto, Japan Model: UV 1800)

Sprayview (Make: Proveris Scientific, USA), Spraytec (Make: Malvern Instruments, UK), Surface tension meter (Make: Culture Instruments, Bangalore, India).

Procedure

The absorbance of placebo, standard and sample solution was measured at 635nm against the blank solution.

Calculation

The % w/w Avicel pH RC 591 was calculated by using the following formula;

$$\%\ w/w\ Avicel = \frac{A_T}{A_S} \chi \frac{Std.\ wt}{250} \chi \frac{1}{25} \chi \frac{250}{Spl.\ wt} \chi \frac{25}{1} \chi \frac{P}{100} \chi 100$$

where, AT is absorbance of sample preparation, AS is absorbance of standard preparation, Std wt is weight of working standard in mg and Spl wt is weight of sample in mg.

Results

Method development

The optimization of the method was done by varying the critical method parameters like Avicel concentration, temperature, reagent concentration, heating time etc. Avicel being insoluble in water didn't give reproducible results. It may be because of the non-uniformity of the sample during the second dilution. 70% orthophosporic acid was used as a diluent to solubilize the polymer instead of water as a diluent. This resulted into a consistent and reproducible absorbance at 635 nm. The wavelength maximum was selected after scanning the solution in the entire UV visible region. Avicel does not have absorbance in the UV region because of the non chromophoric molecular structure. We had derivatized the molecule by reacting with diphenyl amine reagent. The reaction gave a dark blue coloured complex resulting into hyperchromic shift showing wavelength maxima at 635 nm. The optimal detector response was obtained when the reaction was carried out by heating at 90°C for 10 min. The derivatization reaction takes place between Avicel polymer and diphenyl amine in acidic medium (70% orthophosporic acid) at the elevated temperature of 90°C.

Method validation

The described method has been successfully validated for parameters like specificity (selectivity and forced degradation study), LOD (limit of detection) and LOQ (limit of quantification) linearity, accuracy, precision, solution stability and robustness study.

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Specificity (Selectivity and FD)

The Specificity of the method was proved by scanning and measuring the absorbance of diluent, Placebo solution, Standard solution and Sample solution at 635nm for evaluating any interference of diluent and placebo solution at the selected wavelength. During the specificity no interference observed from the diluent and placebo solution at detection wavelength 635nm. Based on these observations the method is found to be selective for Avicel at the selected wavelength.

FD study was performed to prove the specificity of the method and to evaluate the stability indicating nature of the method. Diluent, sample and placebo was exposed under relevant stress conditions viz. heat, light, temperature/humidity, acid, base and peroxide (Table 1) and the exposed samples were analysed as per the method. The absolute % degradation of sample was determined (Table 2). During the FD study, it was observed that, treated diluent and placebo by various FD conditions did not show any interference on quantification of Avicel at the detection wavelength 635nm.

Table 1: Forced degradation study used conditions.

Condition	Degradation Condition	Exposure Period
Thermal degradation	60°C	For 2 d
Photolytic degradation	1.2 million lux hours and 200watt hrs./m^2	27 h
Humidity degradation	40°C/75% RH	For 7 d
Acid degradation	1N HCl	For 2 h
Base degradation	1N NaOH	For 2 h
Peroxide degradation	3% H_2O_2	For 2 h

Table 2: Forced degradation study results.

Stress Condition	% Assay (mg/g)	% Degradation
Untreated sample	19.84	NA
Thermal degradation (60ºC, 2 d)	19.56	1.4
Photolytic degradation	19.23	3
Temperature/Humidity degradation	19.73	0.5
Acid degradation (1N HCl, 2 h)	16.83	15.1
Base degradation (1N NaOH, 2 h)	18.32	7.7
Peroxide degradation (3%H_2O_2, 2 h)	16.59	16.4

LOD and LOQ determination

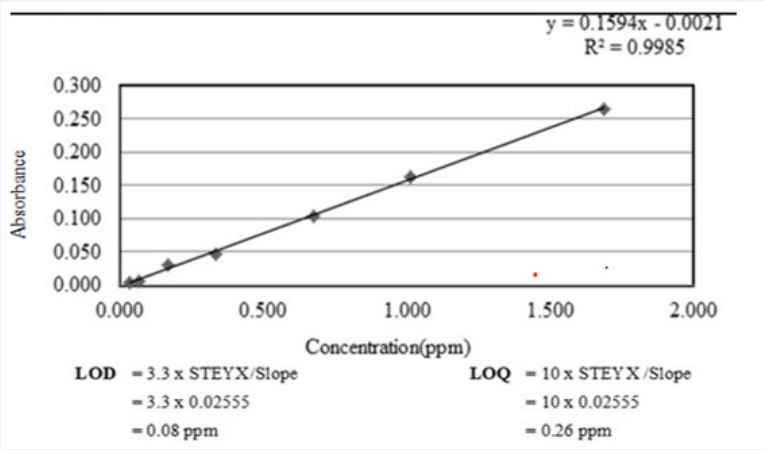

Figure 2: LOD and LOQ Study of Avicel pH.

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The LOD is the point at which the signal from the analyte is equal to three times the noise in the measurement. The LOQ is the lowest concentration of analyte that can be determined with acceptable precision in sample matrices. A series of low concentrations from 0.034 µg/ml to 1.686 µg/ml for Avicel were prepared based on standard response and the absorbance was recorded in triplicate. The calibration line curve was prepared for absorbance vs concentration. From the calibration curve slope, intercept and correlation coefficient along with the STEYX was determined for the calculation of LOD & LOQ values (Figure 2). Based on the response, the established LOD and LOQ values of Avicel are 0.08 µg/ml and 0.26 µg/ml respectively. The Correlation coefficient (r) for both LOD and LOQ was found to be 0.999.

Linearity

Linearity is the ability of the method to produce test results that are proportional, either directly or by a well-defined mathematical transformation to the concentration of analyte in samples within a given range. The method linearity was demonstrated by preparing solutions over the concentration level ranging from 2 µg/ml to 4 µg/ml. Linearity graph of concentration vs absorbance of analyte was plotted. The correlation co-efficient between concentration & absorbance and y-intercept of the correlation plot was evaluated. The linearity study data is reported in Table 3 along with the linearity graph (Figure 3). The method showed a good linearity over the concentration level from 2 µg/ml to 4 µg/ml. The Correlation coefficient (r) was found to be 1.000 demonstrating the linearity within the specified range.

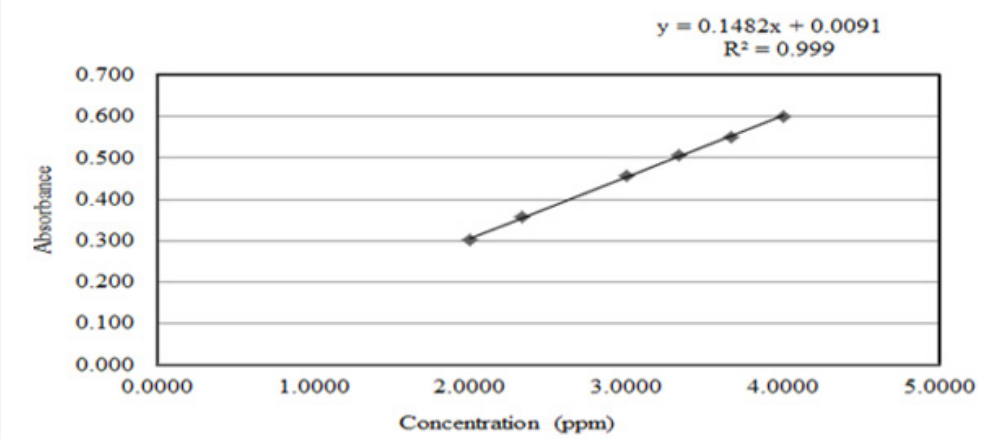

Figure 3: Linearity of Avicel pH.

Table 3: Linearity study results for avicel.

Linearity Level	Linearity level (in % Considering Sample Concentration)	Avicel	
		Conc. (µg/ml)	Absorbance
Level – 1	60	2.0045	0.302
Level – 2	70	2.3386	0.358
Level – 3	90	3.0067	0.457
Level – 4	100	3.3408	0.508
Level – 5	110	3.6749	0.551
Level – 6	120	4.009	0.601
Slope		0.1482	
Intercept		0.0091	
Correlation Coefficient (r)		1	

Precision

The system precision was performed by measuring the standard absorbance in six replicates and calculated % RSD of results is 0.3. The method precision study was performed by measuring the absorbance of six different samples of same batch and calculated % RSD of results is 0.65 (Table 4).

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Intermediate precision/ruggedness

To evaluate the intermediate precision (also known as Ruggedness) of the method, Precision was performed through different analyst, on different day by measuring the absorbance of a six different samples of same sample batch (used in method precision) and calculated % RSD of results is 0.98 (Table 4). The ruggedness of method was successfully demonstrated by computing % RSD of results of twelve samples (six of method precision and six of intermediate precision) is 0.88 (Table 4).

Table 4: Method and intermediate precision (ruggedness study) results for avicel from formulated sample.

Sample Solution	Method Precision (Analyst-1)		Intermediate Precision (Analyst-2)	
	Absorbance	mg/g	Absorbance	mg/g
1	0.458	19.66	0.445	19.36
2	0.456	19.8	0.454	19.63
3	0.458	19.76	0.464	19.79
4	0.451	19.5	0.444	19.45
5	0.462	19.56	0.453	19.63
6	0.454	19.79	0.452	19.29
	Average	19.68	Average	19.53
	EV	0.1275	STDEV	0.1914
	% RSD	0.65	% RSD	0.98
	Overall Average	19.6		
	Overall STDEV	0.1735		
	Overall % RSD	0.88		

Accuracy (Recovery)

Pure Avicel API was added in placebo at LOQ, 50%, 100% and 150% level of sample concentration and prepared spiked sample solutions as per described method and measured the absorbance's of each sample to calculated the recovered amount, % recovery, mean % recovery and % RSD (Table 5). The recovery results obtained at LOQ, 50%, 100% and 150% levels are 89.0%, 99.6%, 100.7% and 100.0% respectively with %RSD of recovery 4.45%, 1.87%, 1.87% and 1.71% respectively demonstrating the good recovery of this method.

Table 5: Accuracy (recovery) data for avicel.

Accuracy Levels in %	Amount Added (mg / ml)	Amount Recovered (mg / ml)	(%) Recovery	Mean Recovery	% RSD
LOQ	0.00034	0.00032	93.9	89	4.45
	0.00038	0.00034	89.6		
	0.00039	0.00032	83.7		
	0.00034	0.0003	90.2		
	0.00032	0.00027	84.9		
	0.00037	0.00034	91.7		
50%	0.00166	0.00169	101.7	99.6	1.87
	0.00176	0.00174	98.9		
	0.00172	0.00169	98.3		
100%	0.00329	0.00325	98.5	100.7	1.87
	0.00325	0.00331	101.9		
	0.00326	0.00331	101.6		
150%	0.00496	0.00495	99.8	100	1.71
	0.005	0.00492	98.4		
	0.00491	0.005	101.8		

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Solution stability

The standard solution and sample solution were prepared as per method described and tested on immediate basis as an initial result, and then analyzed after every 4 h up to 20 h against the freshly prepared standard solution and calculated % RSD of results up to 20 h comparing with initial result. The % RSD of results for standard solution and sample solution at 20 h are 1.98 and 1.44 (Table 6), this concludes that the Avicel in standard and sample solution was found to be stable for the period of 20

Table 6: Solution stability data for avicel standard and sample solution.

	Solution Stability of Standard	Cumulative		
Hrs	% Assay of Standard	Average	SD	% RSD
0	100	NA	NA	NA
4	101.5	100.8	1.06	1.05
20	104	101.8	2.02	1.98
	Solution Stability of Sample	**Cumulative**		
Hrs	mg/g	Average	SD	% RSD
0	19.57	NA	NA	NA
4	20.04	19.81	0.33	1.68
20	20.09	19.9	0.29	1.44

Robustness study

As part of the Robustness of UV-Visible spectroscopic method, deliberate change ±3nm in the detection wavelength 635nm was made to evaluate the impact on the method. To prove the robustness of analytical method measured the absorbance of five replicates of standard solution at 632nm and 638nm and calculated % RSD are 0.33 and 0.16 respectively.

Marketed sample analysis:

Different APIs and market formulated samples like tablets, ophthalmic suspensions, nasal spray suspensions was successfully analysed by this method without any interferences from different API's and excipients (Table 7).

Table 7: Commercial sample analysis data by described method.

Product category	Product Name	Make	Batch No	Result %
Excipient	Avicel RC 591	Dupont, USA	D1709C	99.9
Excipient	Microcrystalline cellulose	Asahikasei, Japan	K662	93.9
Excipient	Sodium Carboxy methyl Cellulose	Vasa Pharmachem, India	SWSR160103	55.17
Ophthalmic suspension	Catapred	Sunway's, India	TD-1803	0.49
Tablets	Lamivudine	Sava, India	HTE100	44.1
Nasal spray suspension	Nasonex	Merck, Germany	18KTLD510A	1.91

Effect of avicel concentration on the nasal spray suspension products

Table 8: Effect of avicel concentration on nasal spray suspension products.

Test Name	Batch No.1103-22	Batch No.1103-24
	1% Avicel RC591	2% Avicel RC591
Plume Geometry (Plume Angle in°)	54.96	52.6
Spray Pattern (Ovality ratio at 30 mm)	1.345	1.17
Spray Pattern (Ovality ratio at 60 mm	1.579	1.127
Surface Tension (dynes/cm)	45.78	53.7
Droplet size (μ)	71.37	80.28

The Spray pattern (ovality ratio), Plume geometry (plume angle), Droplet size distribution and Surface tension measurement are carried out for the evaluation of impact of Avicel on the nasal spray suspension product. Accurate determination of Avicel

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concentration in drug formulation is very critical [20] since it is well-known that Avicel addition leads to larger increases in the formulation viscosity. This in turn affects the surface tension, spray characteristics and drug deposition pattern of the nasal spray formulation. The results for one such study with different Avicel concentration and its impact on critical parameters such as plume geometry, spray pattern and droplet size in nasal spray suspension product are reported (Table 8).

Since the deposition pattern is dictated by the droplet size of the formulation, hence, accurate estimation of Avicel in such formulations assumes critical importance and our present article describes the method for accurate estimation of Avicel from complex formulations.

Hence, estimation methods for excipients appear crucial since any variation in excipients quantity would have a potential impact on the quality and stability of the developed pharmaceutical formulation [14].

Discussion

Excipients such as MCC play a significant role in promoting the manufacturability of drug product, and bioavailability of the drug substance from the drug product. As a consequence, the characterization of excipients must go beyond the simple tests for identity, purity and strength as prescribed in general by the Pharmacopoeia monographs.

The different MCC grades greatly impact on the pellet forming process during the tablet and capsule manufacturing. The moisture content and shape generally changes during extrusion-spheronization process [20]. The biggest advantage of MCC is its compatibility with APIs, inertness, ease of handling, and abundant availability in the market [21]. Recently, we come across one report published in China on the usage of MCC as an adulterant in pasteurized milk. The reported method of estimation of MCC would certainly prove useful in such circumstances.

The uniformity in the chemical and physical characteristics of any excipient is very crucial in the development of robust and consistent pharmaceutical products. It is important to minimize variation between the different batches of excipient, since if there are significant differences between excipient lots used in clinical and commercial drug product lots badly affects the bioequivalence of the drug product. Hence, estimation of excipient concentration is crucial. Vehovec and co-workers investigated the effect of inclusion of MCC on the stability of APIs, such as Perindopril erbumine and Enalapril maleate.

The moisture content of MCC as per European Pharmacopoeia should not exceed 7.0 % (m/m) since it affects the stability of moisture-sensitive drugs. The stability of medicinal product is more with larger particle size of MCC. It is observed that, with higher content of Avicel, the disintegration time of tablets is shortened. With lower concentration of MCC, the tablets become plastic with less hardness. This shows the importance of using the right concentration of MCC and its accurate estimation from various pharmaceutical products [22].

In Biotechnology industry, MCC (Avicel PH-101) has been successfully used as a delivery carrier of recombinant protein-based antigens in animal models [23]. The immune response of the Avicel absorbed antigen was found to be increased with increasing Avicel particle concentration, confirming its suitability as a better immunosorbent for vaccine systems. MCC nanoparticles are found to be effective in removing organic contaminants and matters from water [24]. The MCC based nanogels with acrylamide and acrylic acid are promising adsorbents for the removal of organic pollutants as well as heavy metals [25].

Chemical derivatization is a process by which the compound of interest is converted to compounds with different spectral properties. One of the primary step of chemical derivatization includes the use of a derivatizing agents in molar excels of analyte so that there is complete conversion of the analyte in question. The derivatized analyte thus formed, have chromophores which will have absorption in the visible region making its detection feasible. The process of chemical derivatization can also be applied to molecules/analytes that have poor absorption in the UV region (200-280 nm) with significant interference from compounds that are either impurities or degraded products of compounds or excipients. Hence a colorimetric method of estimation will always have advantages over UV/Vis method of estimation using spectrophotometer [26].

Accurate determination of Avicel concentration in drug formulation is very critical [20] since it is well-known that Avicel addition leads to larger increases in the formulation viscosity. This in turn affects the surface tension, spray characteristics and drug deposition pattern of the nasal spray formulation. The results for one such study with different Avicel concentration and its impact on critical parameters such as plume geometry, spray pattern and droplet size in Nasal spray suspension product. Since the deposition pattern is dictated by the droplet size of the formulation, our present article describing the estimation of method of Avicel in such formulation assumes critical importance [14,27,28].

Conclusion

The proposed HPLC method was found to be simple, specific, precise, accurate, rapid and economical. The developed chromophore is highly selective with a significantly different λmax from that of chromogenic agent. UV- Visible spectrophotometry is simple and sophisticated tools of the analysis. Using diphenylamine as derivatizing reagent the detection was carried out at 635 nm. The validated economical method was successfully applied for forced degradation study of Avicel in different pharmaceutical formulations and method is found to be selective and stability

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indicating. Very low concentrations for LOD and LOQ were found 0.08 µg/ ml and 0.26 µg/ ml respectively with linear regression coefficient of 0.9993. The linearity range of Avicel was proved from 2-4 µg/ ml with linear regression coefficient of 1.0000. The % RSD of precision study is less than 2% indicating accuracy and precision of the method. The mean percentage recovery at LOQ level is 89% with % RSD less than 5% and at 50%, 100% and 150% levels in between 99-100% with % RSD less than 2%. For Q1, Q2 sameness study successfully the quantification of Avicel from different pharmaceutical formulations like tablets, capsules, nasal suspensions and ophthalmic suspensions etc was performed by present validated method. The accurate quantitation of Avicel will help us to specify the important functional tests like spray pattern, plume geometry and droplet size distribution from patient point of view. Different grades of Avicel like RC-591, CL-611, RC 591F are also successfully quantified from different pharmaceutical formulations. The method can also be extended for the quantitation of MCC and sodium CMC excipients separately from different pharmaceutical formulations.

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