Report on One Day Symposium

Simulation for Pharmaceutical Manufacturing

21st September 2022

Date & Time: 21st September, 2022, Time: 10.00 AM

Organized by: Indian Pharmaceutical Association (IPA) Telangana State Branch, co-hosted by ALTAIR, India in co-ordination with Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, (Sponsored by Exhibition Society, Tarnaka, Secunderbad) (Approved by AICTE & PCI, B.Pharmacy – NBA accredited , Affiliated to Osmania University.

For this event, Total number of participants registered were 208 and the number of participants attended the event were 151

The programme started at 10.00 am by lighting of lamp by the speakers and guests of the program followed by a prayer song "Vandemataram" by Ms. Lisa Patel and group. Dr. Hyma has introduced Dr. B. Prabha Shankar sir, President, IPA, Telangana State branch, Chairman, SNVPMV and requested him to present a welcome note on the programme.

Dr. B.Prabha Shankar sir, on behalf of IPA – TS branch & SNVPMV extended a warm welcome to the key note addressee of this Symposium, 'Simulation for Pharmaceutical Manufacturing', Dr.V.Venkateswarlu, Managing director, Neuheit Pharma Technologies Pvt Ltd., & welcomed the entire official team of Altair India Ltd, specially Mr.Ajay Pandey, Head, Marketing, Altair, India. Sir, extended warm welcome to Mrs. Sridevi Challa, Group Head-formulation division, Novartis; Mr. Senthil Arumugam, Director of APAC Sales-DEM Technology, Altair, United Kingdom, Dr. Ravi Pyaraka, Founder, Chairman & MD, Pharma DEM Solutions Pvt Ltd., Mr.Mohan Nainegali, Product Manager, EDEM, Caezen Technologies, Dr.A.Ratna Kumar, Assoiate Professor of Mech. Engg., IIT Madras, and finally sir extended his welcome to all the members of Altair, IPA, governing body members & faculty of SNVPMV and most importantly to all the delegates who have attended the symposium from various facets of pharmacy including pharma industry, regulatory and academics, and also to Sri Hanumanth rao garu, the former director, Drugs control Administration and addressed all the attendees. In his welcome note, Sir said that the three organizations, IPA, Altair and SNVPMV were jointly organizing this event and feel fortunate and

honoured to be associated with Altair for the first time and thanked Altair for bringing experts for this event.

In his welcome note, Sir has given the importance of processing of particulate matter in pharmaceutical industry. Sir, explained that the particulate materials are ubiquitous but exhibit mechanical behavior during formulation which lead to diverse set of problems like loop dosing control, size and component segregation unwanted attrition, agglomeration, non uniform mixing etc which increases the time and manufacturing costs. These problems can be overcome beyond the physical testing where the EDEM (Experts in Discrete Element Modeling) simulation takes its place. Sir gave a brief introduction on this EDEM which simulates the accurate behavior of particulates to obtain new and deeper understanding on the process and product development, get process quality check etc. Sir, introduced Dr.V.Venkateswarlu, Managing director, Neuheit Pharma Technologies Pvt Ltd., as the man of bioequivalence, & welcomed to deliver the key note address of the programme.

Dr. V. Venkateswarlu, Managing Director, Neuheit Pharma Technologies Pvt Ltd., started his speech with the shloka, "Gurubrahma, guruvishnu…" and welcomed all the enthusiastic delegates who have come to attain knowledge on new technologies through this symposium. Sir, thanked his beloved senior Dr. B. Prabha Shankar sir for inviting him to the programme. Sir, told that the leaders in pharma industry like Pfizer, Novartis etc have been using this type of simulation software and it is not yet introduced in all the generic pharma companies. Sir, emphasized that composition is easily optimized but real problem lies in the process which varies from the batch of 10000 tablets to the batch of one lakh tablets where the composition is same but process varies. He explained simulation for pharmaceutical manufacturing methodologies which are of two type of models – Large scale continuum model also called computational fluid dynamic model and Discrete Element method. He then gave a brief insight on the expectations from the symposium as it is a emerging technology, the presenters should educate the participants on the fundamental concepts, applications and power of this scientific advancement y showing some practical examples to understand the concept easily.

Dr. P. Hyma introduced Mrs. Sridevi Challa, Group Head-Formulation Division, Novartis to deliver the lecture on "Granulation &Tablet Coating, how Sandoz does it?" The young and energetic lady hit the dais with the round of applause by audience and started her lecture by

thanking Dr. B. Prabha Shankar sir & Dr. V. Venkateswarlu sir for their valuable introduction of EDEM technology which made her job easy and expressed her gratitude to share the dias with the visionary leaders.

Madam shared her experiences working with MNCs like Dr.Reddy's and Sandoz Novartis who supported her in deploying the emerging new technologies in data sciences and digital pharmaceutical development in various method developments and high level 6 sigma processes in understanding the various unit operations in tablet manufacturing and coating. Madam quoted few points of Dr. V. Venkateswarlu sir's presentation to understand the selection of right materials, right people & process variable in large scale manufacturing of tablets.

Madam emphasized on various problems in manufacturing the tablets in large scale and explained how the Sandoz introduced the software in manufacturing of various unit operations and specially in tablet coating which is dependent on many processes and machinery variables. Madam explained various in-silico modeling approaches in tablet coating by DEM in a series of stages like liquid jet breakup, atomization of coating formulation, droplet transport, wetting, drying etc. Madam gave a brief insight on the benefits associated with DEM platform in overcomimg the processing problems in tablet coating by usng in-silico modeling approach. Madam described about the input variables like segregation index, displacement curve & coefficient variables to get the quality output and to overcome the problems of coating. It was overall, extremely helpful and interesting to all the attendees. The session was followed by tea break for 15 min.

After a high tea and refreshments, the session was restarted with full of energy and enthusiasm. Dr. P. Hyma introduced Mr. Senthil Arumugam, Director of APAC Sales-DEM Technology, Altair, United Kingdom, and requested him to deliver his talk. Mr. Senthil Arumugam presented on the topic entitled, 'Discrete element modeling for pharmaceutical manufacturing process, Case study: virtual optimization of bin blending process.' Sir gave a brief overview on Altair, which is accommodated with 3000 plus engineers and scientists with an annual turnover of about 532 million US dollars and working with a vision of 'Transforming customer decision making with simulation, data analytics, and high performance computing'. Sir explained the contexts and challenges of all the pharmaceutical products in particulate states such as stress state dependent, strain rate dependent, sensitive to ambient conditions such as humidity, temperature etc and described how the EDEM technology helps to solve the problems associated with particulate

materials in pharmaceutical industries. He emphasized the uses of EDEM simulation technology for fundamental investigation of process mechanics at macro and micro scale, virtual prototyping and optimization of equipment and process operation. Sir explained the Discrete Element Method (DEM) which is used to model the complex macro mechanical behavior of bulk solids using micro mechanical parameters. Sir gave a brief insight on world first powder material model data base which reduces time and resource requirements for powder modeling. Sir, described the benefits of EDEM which allows the users to obtain the new and deeper understanding of the processes, inform design and scale up, reduce dependence on physical prototyping and help to get the products to the market quicker and also stated the applications of EDEM in storage, conveying, mixing, granulation, tableting, tablet coating etc. Further, sir presented a case study of Client Novo Nordisk, on Pneumatic conveying to 'Understand the effect of operational parameters and powder properties on system performance' and concluded that the ongoing coupled EDEM- Acusolve modeling at Novo Nordisk is producing valuable insight into complex mechanics of the pneumatic conveying process which can be used to inform plant operation. Sir also explained the pharmaceutical industry applications of pneumatic conveying of Dry powders, Dry powder inhalers etc. Sir then presented the DEM simulation of registration Bin lender- with reduced tilt angle (15^{o}C), reduced fill level, and its risk assessment etc to attain final blend uniformity with the help of pictures and case studies. On the whole the session went enthusiastically and found to be more informative.

Dr. P. Hyma introduced Dr. Ratna Kumar Annabattula, Associate professor, Department of Mechanical engineering, IIT Madras to deliver his lecture on topic, "Discrete element modeling for pharma industry". As Dr. Ratna Kumar sir is an engineering specialized person, he described that whole universe is containing the granular materials in various ways and depicted the flow properties of granular materials used in pharmaceutical industry by showing the general examples like hand full of paddy grains, pebbles, train boarding and beach and correlated the picture in a very interesting way with the granular mechanics, how geometry and porosity effect the granular mechanics. Sir explained the complex mechanical behavior of different materials and problems that arise during their movement, processing etc and emphasized the importance of EDEM which work on every particle by potential logarithm on the basis of Newton's second law to know the nature of each and every particle which not only reduces the cost of production but also helps to overcome the toughest processing problems in pharmaceutical manufacturing. Sir explained

difference between simulation and animation with a video example and has shown Cundall photo who proposed DEM method 40 years ago where it need sophisticated computers to run this DEM. Sir explained about the conduction of unit operations in capsule manufacturing and other various unit operations used in pharmaceutical industry with EDEM software and also gave a brief insight on working of capsule conveyer belt and sieve analysis by using EDEM for process optimization. Sir quoted explained by taking the example from Mr. Senthil lecture about the tablet coating and mass loading on tablets how we can use the simulation to know mass overcome the segregation and aggregation of materials and he explain about Segregation index/ mixing index and how to get the logarithm data through EDEM to overcome this serious issue in various formulations. Finally he mentioned the effect of various parameters to get the quality data through EDEM technology by one saying **"**Garbage in is garbage out**"** if you don't put the right things in, you don't get the right thing out. Hence, the process parameters need to be calibrated to get the accurate results. He concluded his lecture with future aspects of EDEM about the selection of suitable parameters, calibration of the parameters and extended the future aspects of machine learning, working of EDEM in day to day work. Sir, concluded his lecture by thanking Altair and IIT madras by supporting his work through funding.

Dr. P. Hyma introduced Dr. Ravi Pyaraka**,** Chairman & MD, PharmaDEM solutions Pvt.Ltd, doctorate in management studies with over 25 years of experience working in various MNCs of IT, Healthcare, BioTechnology and requested to deliver his talk. Sir, gave a brief overview about PharmaDEM organization which was aimed to set up its precedence as a consulting and services organization providing digital twin solutions at early stage and late stage of Drug Discovery & Drug Development life cycle in Global Pharmaceutical & Bio Technology Industries. Dr. Ravi Pyaraka in PharmaDEM works tirelessly on establishing a strategic plan that accounts for the needs of the Pharma customer, Work with organization influencers to build a mutual profitable positions by instilling the technology transformations, digital innovation methods which controls and optimizes the processes. Dr. Ravi Pyaraka introduced Dr. Ravi Shekar Ananthula, Executive Director, who has more than 17 years of cross functional experience in synthetic chemistry, Computational chemistry, Solid state chemistry, Process chemistry, Pre-formulation, Absorption modelling, Predictive toxicology, Drug device development and Lab automation etc and requested to deliver the talk on topic, " How DEM and chemistry modeling helping pharma industry". Dr. Ravi Shekar Ananthula explained about the PharmaDEM which is a physics and chemistry

modeling expert company for drug design and development. PharmaDEMhas unique capability of providing integrated modeling and solutions of all scales enables the full integration of knowledge during product development. Sir explained on Molecular Modeling which includes atomistic level description and mimicking the behaviour of molecules, Simulating the molecule behavior with the equations of quantum and classical physics, Optimizing the solutions at molecular level to have full control on formulation chemistry. Sir has given the benefits of modeling in formulation development- which is used to determine the compatibility of each component in the formulation, rational selection of excipients for better bioavailability and manufacturability without affecting the API stability, Selection of right concentration of excipients for API stability. Sir gave a detailed note on Solubility Model accuracy-and its applications which include used as screening tool to guide initial experiments (rather than experimental screening), high performance computing to screen large solvent spaces, synergistic effects, anti-solvent effectivess, temperature dependence, guide experiments and additional (higher accuracy) models to explore promising spaces. Sir explained on SoluDEM-Solubility Modeling Platform, which gives knowledge on solvents where 1900 solvents can be screened in 48hours at multiple temperatures, and binary mixtures. Sir added that these models are 85% accurate when tested on 2600 experimental data points and are applicable to small molecules, small peptides, oligonucleotides, etc. Other applications include: quick alternate strategies without spending the time and experiments, quick decision based on in-silico results which saves the experimental time and resources. Sir briefed on API-chemistry modelling: Polymorph screening; API-Salt screening, impurity rejection, Solvents, conditions for crystallization, etc PharmaDEM can provide guidance regarding-Final dosing and alternate dosing approaches, optimal and alternate drug formulations, drug-drug interactions and other safety concerns, drug absorption. DEM and CFD modeling is a powerful tool, accurately analyzes the behavior of granular materials such as dust particles, tablets and capsules. DEM is a powerful solution used to model pharmaceutical manufacturing processes such as coating, drying, granulation, solids mixing using digital twins.

PharmaDEM solution approach is to emulate the environment by creating digital twin through simulations (both material compatibility and material interactions to access the overall process behavior) for better production results which would result in low wastages, & increased production rate through optimum process parameters. Sir concluded that PharmaDEM solution can provide

solutions to address potential manufacturing challenges or failures such as poor flowing tablet formulations, which lead to low tablet yield or non-uniformity in dosage or segregation issues, etc.

Dr. P. Hyma introduced Mr. Mohan Nainegali, Product Manager, EDEM, CAEZEN Technologies to deliver his lecture on the topic "Benefits of adopting EDEM for Pharma Industry". His presentation focused more on insights on Oral Solid Manufacturing applications. The aim was to provide simulation techniques from various countries which are being used in this technology of EDEM. It provides virtual platform for stimulating the bulk products or granulating solid products. This technology gives an opportunity to assess performance of equipment through using various optimization techniques. Harvesting computer software and technology along with the model process are currently being focused topics.

Sir has stated the following benefits of simulation:

It helps us to get converted amount of information which is otherwise difficult to find during the process. We get the information about what is happening to tablet inside the equipment. Information related to bulk volume of products, and EDEM also determines the contact between particles and the forces involved in collision of two particles. EDEM requires inputs on material which is being dealt with API and excipients interactions. It involves studying various processes involved during manufacturing viz., mixing, blending, drying, coating etc. and also study the behavior of particulate systems. The data is visualized using images and videos.

Mixing was the first process studied where EDEM played a role in simulating mixing of wet particles and agglomeration of particles in unit operation process. Particles size distribution also played a crucial factor in mixing process.

Finally, Sir concluded that, EDEM technology is a new technology being adapted worldwide to reduce wastage of materials during the manufacturing process and get detailed insights on the information which is difficult to obtain otherwise.

The session is continued with Question and Answers. Student volounteers have collected the questionnaire slips from the audience and are handed over to Dr. P. Hyma. Dr. P. Hyma has asked the questions from the obtained slips to concern speaker from the questionnaire slips. All the questions were patiently answered by the speakers and clarified the doubts with lot of patience

making the session, both informative and interactive. It was overall, a very excited, novel and interesting session to all the attendees.

The session came to the end with closing remarks by Dr. V. Venkateswarlu sir. Sir thanked all the speakers who enlightened the participants well with new technology and said that 80% of his expectations were met. He was convinced with wide utilization of EDEM in various fields of pharmaceutical manufacturing, and conveyed the message that every teacher and student should percolate the simulation in academic practice. Guests were felicitated by Chairman, Dr. B. Prabha Shankar and other dignitaries.

The function was concluded with Vote of thanks by Mr. Ajay Pandey, Head Marketing, Altair, India. Sir thanked Dr. B. Prabha Shankar, President, Indian Pharmaceutical Association, TS branch & Chairman, SNVPMV for his visionary thought to enlighten the gathering with new software. Sir acclaimed Dr. N. Srinivas, Director, SNVPMV and as the man behind the show who provided good hospitality and support to make the event success. Sir also explained the key points from each speaker's note and finally thanked Sri Sainath dayaker Hon.Secretary, SNVPMV, Mr. Pandhuranga Rao, MD Altair India, Dr. T. Saritha Jyostna, Principal, SNVPMV, Dr. T. Mamatha Vice principal, SNVPMV for their support. Finally, Sir, appreciated Dr. B. Prabha Shankar sir, President, IPA, Telangana State branch, Chairman, SNVPMV for his tireless effort in initiation and making this event a grand success. The session was ended with national anthem.


One Day Symposium


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In Co - Ordination with
PHARMACEUTICAL MANUFACT
21st September 202
SAROJINI NAIDU VANIT
VIDYALAYA
Keynote Add
Dr. V. VE
MD,Neuhe
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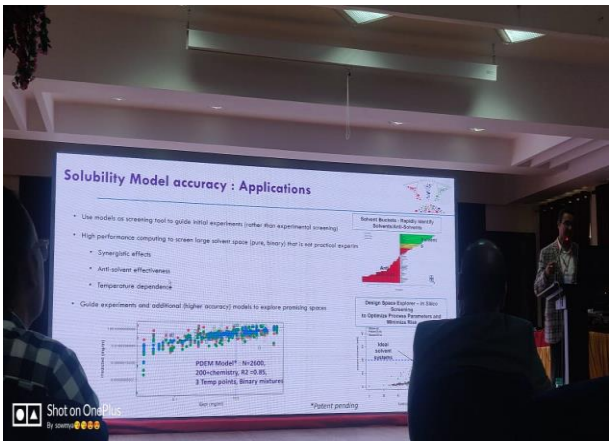
AJAY PANDEY
Dr. RAVI
Founder
& MD, P
Solution
Dr. A. RATNA K
Associate Profe
of Mechanical
IIT Madras


CURRENT APPROACH OF PROCESS OPTIMIZATION
Application of QbD principles and optimization of scale independent parameters a D scale for the process used for manufactu formulation
Scale up of the process using sc principles – such as calculations based o ns
There is no complete process ding and failures du commercializa and djustment ocess parame mercial le is with 3 valid ches


Contents


About Altair
$532M
FY21 Revenue
3,000+
Engineers, Scientists, and Creative Thinkers
1985
15,000+
Customers Globally
86
Offices in 25 Countries
150+


Granular Materials are Ubiquitous!
Source: WWW


Solubility Model accuracy : Applications
Use models as screening tool to guide initial experiments (rather than experimental screening)
High performance computing to screen large solvent space (pure, binary) that is not practical experim
Synergistic effects
Anti-solvent effectiveness
Temperature dependence
Guide experiments and additional (higher accuracy) models to explore promising spaces
PDEM Model* : N=2600, 200<chemistry, R2 >0.85, 3 Temp points, Binary mixtures
*Patent pending
Shot on OnePlus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