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DISPERSIBLE FORMULATION MAKEUPS FOR PEDIATRIC USE: A REVIEW

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ABSTRACT: Childhood is characterized by periods of rapid growth, maturation, and development. There is a change in the magnitude of the dose required during childhood and adolescence. Thus, Paediatric practice requires a range of dosage forms that are acceptable at different ages and abilities and a range of strengths or concentrations allowing administration of the correct age-related dose. Literature shows that a significant percentage of products suitable for children have inadequate dosing information and the products licensed for children, dosage forms are unsuitable for the intended ages. The development of multiple dosage forms for different ages will rarely be commercially viable and liquid formulations, which can be given to a broad age group, present particular pharmaceutical challenges. However, if there is the commercial incentive of a large market for common illness such as pain or vomiting a complete and varied portfolio of products can be made available. Dispensible drug delivery treatment is one of the breakthroughs that modify the conventional dosage forms (swallowing and chewing) for infants and children. In pharmacology and clinical pediatrics, the focus is on the active drug substance (or active pharmaceutical ingredient (API)) when determining dosage, clinical effects, and adverse drug reactions. However, the formulation is fundamentally important since it determines, in practice, whether the dose can be successfully delivered to the pediatric patient. Moreover, it is important to consider the formulation excipients and the potential for any adverse effects in this potentially vulnerable age group.

INTRODUCTION: The development of formulations, which are appropriate for children, present significant challenges to the pharmaceutical industry. The age at which children take tablets or capsules is a factor of importance to their safety so that inadvertent inhalation and choking are avoided but is also of great importance to manufacturers.

Tablet formulations are generally easier and cheaper to develop, manufacture, transport, store and dispense than liquid medicines. There is little information in the literature, but it is generally believed that traditional tablets may be accepted by children of school age, although this will depend on the size and shape of the tablet and patient factors such as the taste of liquid medicine alternatives.

Advances in pharmaceutical technology have resulted in the development of many different types of tablets such as melts, chewable and orodispersible tablets, and it is technically possible that appropriate tablet formulations could be made available for children of most ages but at a cost¹.

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Pediatric formulations must allow accurate administration of the dose to children of widely varying age and weight. While the oral route will be preferred for long term use and the intravenous route for the acutely ill, many of the dosage forms designed for adults, such as orodispersible tablets, buccal gels, and transdermal patches, would also benefit children if they contained an appropriate pediatric dose. The age at which children can swallow conventional tablets is of great importance for their safety. Liquid medicines are usually recommended for infants and younger children, so the ability to mask the unpleasant taste with sweeteners and flavors is crucial.

There are various reasons for the formulation of drugs into appropriate dosage forms; one of the most important relates to the accurate measurement of the dose. Many active drugs are very potent and only require milligram, or microgram amounts to be administered. For children, the amount of drug required for the dose varies with age and weight. Active drugs must be diluted in a vehicle which allows accurate and convenient dose measurement. Active drugs must also be protected during their shelf life from degradation, for example by oxygen and humidity and, when administered orally, may require protection from degradation by gastric acid. It may be necessary to conceal taste and smell and to produce liquid preparations of insoluble or unstable drugs. There may be a requirement for rate-controlled action, or optimization of delivery of topical or inhalational drugs and those delivered by injection must be sterilized².

A wide variety of solid dosage forms are now available including powders, *e.g.*, Viracept® oral powder (nelfinavir mesylate, Pfizer), granules, *e.g.*, Singulair® oral granules (Montelukast Na, Merck), sprinkles (*e.g.*, Depakote®) and sprinkle capsules (Divalproex Na, Abbott). These are usually mixed with specified food or drink and are easy to swallow. Taste is again important; there is a risk of incomplete ingestion and consequently a reduction in the dose given. Potential for technical challenges include powder processing, packaging, stability, and dose extraction³.

A variety of modern tablet preparations is available such as fast-dispersing dosage forms (FDDFs), for example, Calpol Fast Melts® (Pfizer Consumer

Health), Nurofen® Meltlets (Crookes Healthcare), Benadryl® orodispersible tablets. None of the products currently has a license for children less than 6 years of age, primarily due to the dose strengths available. These products are placed in the mouth where they 'melt' on the tongue in a small amount of saliva or can be dispersed in a small amount of liquid on a spoon. They are easy to administer providing that taste is acceptable, and they provide accuracy of dose. However, many of these technologies are proprietary and consequently will require licensing agreements. Development costs are higher than for conventional oral dosage forms. Examples include Zydis™ (Scherer), OralSolv™ (Cima), WOWtab™ (Yamanouchi), Films (LTSLohman).

Formulation Aspects of Various Dispersible Tablets:

Ibuprofen: Chowdary *et al.*, (2000) formulated dispersible tablets of Ibuprofen employing potato starch, primo gel, microcrystalline cellulose (MCC) and pre-gelatinised starch (PGS). Tablets were evaluated for the content of active ingredient, hardness, friability, disintegration time, uniformity of dispersion and dissolution rate. Tablets were formulated employing primo gel as internal and external disintegrants. It was observed that tablets formulated employing potato starch as internal disintegrants and Primo gel and PGS as external disintegrants fulfilled all the official and other requirements of dispersible tablets. These tablets also gave a rapid and higher dissolution rate than the other formulations as well as conventional (marketed) tablets. The dissolution of ibuprofen from the tablets formulated followed first order kinetics. They concluded that the dissolution rate of ibuprofen; a poorly soluble drug could be increased by formulating it as dispersible tablets⁴.

Nimesulide: Rao *et al.*, (2002) have reported about the development of dispersible tablets of Nimesulide using Primojel as dispersing agent with starch, lactose, and dicalcium phosphate as diluents were prepared and evaluated and compared with commercial dispersible tablets. The formulations with starch and lactose as diluents showed fast and rapid dissolution when compared to that of commercial tablets whereas the formulations with dicalcium phosphate as diluent showed less dissolution rate⁵.

Flurbiprofen: Manvif *et al.*, (2005) reported about the preparation of dispersible tablets of Flurbiprofen, formulated by employing different disintegrants, such as pregelatinized starch (PGS) microcrystalline cellulose (MCC) and Sodium starch glycolate containing different concentrations of disintegrants, starch paste as a binder.

The dispersible tablets of Flurbiprofen gave fast & rapid dissolution when compared to a Conventional marketed tablet of the same drug. Dispersible tablets formulated by employing sodium starch glycolate gave the fastest dissolution of Flurbiprofen the formulated dispersible tablets are more convenient for pediatric use ⁶.

Oxcarbazepine: Fast dissolving tablet of Oxcarbazepine containing Avicel pH 102 as a diluent and Ac-Di-sol as a super-disintegrant by wet granulation process has been reported by Malke *et al.*, (2007). They have evaluated all the formulations on the basis of hardness, friability, weight variation, wetting ability, disintegration time and dissolution rate and they concluded that formulation containing 12% Ac-Di-sol, 25% Avicel PH 102 and 8.5% starch as a binder was found to have a good hardness of 4-4.5 kg/cm², disintegration Time of 28 ± 5 s and drug release of not less than 90% within 30 min ⁷.

Piroxicam: Snehalatha *et al.*, (2009) have reported about the development of a Piroxicam dispersible tablets using various natural disintegrating agents like Isapgol husk, tragacanth by direct compression technique to get required theoretical release profiles. They have shown that the formulation prepared by direct compression F5 exhibits better dissolution, disintegration at low concentration of natural disintegrants ⁸.

Etoricoxib: Bhatt *et al.*, (2009) have reported about the development of Etoricoxib dispersible tablets a highly selective cyclooxygenase-2 (cox-2) inhibitor using various super-disintegrants like croscarmellose sodium, and sodium starch glycolate using direct compression technique. They concluded that dissolving tablets of the poorly soluble drug, Etoricoxib, can be successfully prepared with enhanced dissolution, improved bioavailability, and hence better patient compliance and effective therapy ⁹.

Norfloxacin: Kuchekar *et al.*, (2009) reported about the preparation of dispersible tablets of Norfloxacin using natural substances as disintegrants such as *Ispaghula husk* powder, *Cassia tora* powder, cassia tora powder (defatted), and *Cassia nodosa* powder in different concentration by direct compression method. Formulations were evaluated for the standard of dispersible tablets and were compared with marketed products. The study reveals that natural gums used as disintegrants were effective in low concentration ¹⁰.

Olanzapine: In 2009, Patil *et al.*, reported about the preparation of Olanzapine quick dispersing tablets by direct compression method using crospovidone. A 3² factorial design was used in formulating a quick dispersible tablet. The f2 was found to be 72.68 for the developed formulation indicating the release was similar to that of marketed formula ¹¹.

Cefadroxil: Damodharan *et al.*, (2009) carried out studies on the formulation and evaluation of Cefadroxil dispersible tablets. Dispersible tablets were formulated with crospovidone, sodium starch glycolate and croscarmellose sodium as super disintegrants with cefadroxil as a model drug. Various precompression parameters like angle of repose, compressibility index and Hausner's ratio and post compressional parameters like weight variation, thickness, hardness, friability, disintegration time, dispersion time, wetting time, drug content uniformity and *in-vitro* drug release were studied. They have concurred that formulation containing croscarmellose sodium, and sodium starch glycolate showed a decrease in angle of repose with an increase in concentration. The angle of repose was increased with an increase in the concentration of cross-povidone ¹².

Flucloxacillin: Kavitha *et al.*, (2010) worked and reported about the formulation of Flucloxacillin sodium dispersible tablets by wet granulation method using non-aqueous solvents. Super-disintegrants like sodium starch glycolate, pregelatinized starch, DoshionP544D and starch as intra-granular disintegrants and croscarmellose sodium & microcrystalline cellulose as both intra & extra-granular disintegrants were used in various proportions. It was concluded from their results that

F11 satisfies all the requirements of a dispersible tablet with no significant changes in all the parameters¹³.

Aceclofenac: Preparation of Aceclofenac dispersible tablet by direct compression method after incorporating superdisintegrants croscarmellose sodium, crospovidone, and sodium starch glycolate has been reported by Wagh *et al.*, (2010). It was concluded that dispersible Aceclofenac tablets could be prepared by direct compression using superdisintegrants¹⁴.

Diclofenac: Malviya *et al.* have reported preparation of dispersible tablets of Diclofenac sodium using Cucurbita maxima pulp powder as disintegrant by wet granulation technique. Different formulations were prepared with different concentrations of 2.5, 5, 7.5 and 10% w/w) of Cucurbita maxima pulp powder and sodium starch glycolate, and evaluated for physical parameters such as thickness, hardness, friability, weight variation, drug content, disintegration time and drug dissolution. The formulated tablets had good appearance and better drug release properties. Studies indicated that the Cucurbita maxima pulp powder is a good pharmaceutical adjuvant, specifically a disintegrating agent¹⁵.

Lornoxicam: Metker *et al.* (2011) have reported the development of orodispersible tablets of Lornoxicam using KYRON T-314 (Polacrillin Potassium) as a novel super-disintegrant. They have prepared dispersible tablet of Lornoxicam by wet granulation technique using KYRONT-314 as super-disintegrant and menthol as a subliming agent. The study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance¹⁶.

Meloxicam: Recently, it has been reported by Kulkarni *et al.*, (2011) about the preparation of Meloxicam dispersible tablets by wet granulation procedure to improve the therapeutic efficacy under the influence of super-disintegrants such as crospovidone and croscarmellose sodium tablet. They revealed that tablets are containing crospovidone exhibit quick disintegration time than a tablet containing croscarmellose sodium. The fast disintegrating tablets of meloxicam with shorter disintegration time, acceptable taste and sufficient

hardness could be prepared using crospovidone and other excipients at optimum concentration¹⁷.

Ciprofloxacin: Setia *et al.*, (2011) studied on formulation and evaluation of ciprofloxacin hydrochloride dispersible tablets using natural substances as disintegrants. Dispersible tablets of ciprofloxacin hydrochloride were prepared using the natural substance as disintegrants such as *Isabgol husk* powder, alginic acid and agar powder in different concentrations by direct compression method. Dispersible tablets of ciprofloxacin hydrochloride were prepared using direct compression method after incorporating different natural disintegrates. It was observed that all the formulations were acceptable with reasonable limits of the standard required for dispersible tablets. This study reveals that natural gums used as disintegrants were effective and isabgol at a concentration of 5% produce the best dispersible effects¹⁸.

Diltiazem: Jadhav *et al.*, (2011) carried out formulation and evaluation of dispersible tablets of Diltiazem hydrochloride dispersible tablets prepared using superdisintegrants such as croscarmellose sodium (Ac-Di-Sol) and sodium starch glycolate. Formulations were evaluated for the standard of dispersible tablets. It was observed that all the formulations were in an acceptable range with reasonable limits of standards required for dispersible tablets. The study reveals that superdisintegrants used were effective in low concentrations. It was concluded that dispersible tablets with an enhanced dissolution rate could be made using selected superdisintegrants¹⁹.

Ampicillin & Cloxacillin: Abhishek Pandey *et al.*, (2011) formulated and evaluated the physical parameter of the dispersible tablet of Ampicillin & Cloxacillin by direct compression method. Observations made were the faster onset of action minimized, first pass effect improved bioavailability, improved compliance²⁰.

Zidovudine: The studies carried out by Yash Paul *et al.*, (2011) on formulation and evaluation of taste masked dispersible tablets of Zidovudine, an antiretroviral drug commonly used in the treatment of HIV infection. The drug is very bitter in taste and sparingly soluble in water. The purpose of this

research was to formulate and evaluate taste masked dispersible tablets. Dispersible tablets of zidovudine were prepared using croscarmellose sodium (Ac-di-sol) as a disintegrant. Surelease Clear (E-7-19010) (Ethylcellulose Dispersion) in the concentration range of 0.044 mL/tab to 0.052 mL/tab completely masked the taste of zidovudine. The prepared tablet formulations were evaluated for general appearance, drug content, weight variation, thickness, hardness, friability, taste evaluation, mouthfeel, *in-vitro* dispersion time and *in-vitro* dissolution studies. Tablets formulated showed quick disintegration time, which is an important characteristic of dispersible tablets.

Results revealed that the tablets containing taste enhancers and sure lease as binder had good palatability. Oral dispersible tablets prepared using Sure lease 0.044 mL/tablet and Ac-di-sol 6% possessed least disintegration time (18.9), pleasant taste and offered better dissolution profile than that of all other dispersible tablet formulations developed in the present investigation and that of marketed conventional tablet formulations of Zidovudine²¹.

Stavudine, Lamivudine, and Nevirapine: Padmavathi *et al.*, (2011) reported that dispersible tablets were acceptable for use in pediatric HIV patients of ages 1-8 years as a fixed-dose combination (FDC). Studies were carried out on the development of fixed-dose combination dispersible tablets containing Stavudine, Lamivudine, and Nevirapine for pediatric applications to allow administration of the correct weight-related dose in pediatric HIV patients as recommended by WHO. Dispersible tablets were prepared by direct compression method and formulated using different super disintegrants like croscarmellose sodium, sodium starch glycolate, and crospovidone at different concentration levels.

They have studied the effect of superdisintegrants on dispersion time, drug content and *in-vitro* release. The formulation containing croscarmellose sodium showed excellent *in-vitro* dispersion time and drug release as compared to other formulations. Differential scanning calorimetry (DSC) studies exhibited physicochemical compatibility between the three drugs and various excipients used in the tablet formulation²².

Roxithromycin: Ms. Subhasri Mohapatra *et al.*, (2012) carried out studies on formulation and evaluation of Roxithromycin dispersible tablets using primogel powder, kollidone powder, croscarmellose powder, and MCC in different concentration by direct compression method. Formulations prepared were evaluated for the standard of dispersible tablets. Their study conferred that all the formulations were acceptable with reasonable limits of the standard required for dispersible tablets. The study characterized the most effective superdisintegrant²³.

Lamivudine: Sureshbabu *et al.*, (2012) carried out studies on the development of a dispersible fixed-dose combination tablet for pediatric use containing Lamivudine (30 mg), Nevirapine (50 mg) and Zidovudine (60 mg). The tablets were prepared by wet granulation technique and evaluated for various parameters like weight variations, hardness, friability, disintegration time, assay, related impurities, and dissolution profile. The optimized formulation contains 12% of Lamivudine, 20% of Nevirapine and 24% of Zidovudine as active ingredients, 24.8% of lactose monohydrate and 8% of microcrystalline cellulose as diluent, 5.2% of sodium starch glycolate as disintegrant, 1.4% silicon dioxide as glidant, 1.6% sucralose as sweetener, 0.8% strawberry flavour, 1% of povidone as binder and 1.2% of magnesium stearate as lubricant. The optimized formulation had a weight variation < 10%, hardness of 35-50N, percentage friability of 0.15, disintegration time of 55-60 sec, % assay was 102.2% for Lamivudine, 99.9% for Nevirapine and 102.5% for Zidovudine and *in vitro* drug release after 30mins was 100.2 % for Lamivudine, 99.9% for Nevirapine and 100.1% for Zidovudine. Tablets were packed in HDPE containers for stability study. The formulation was stable after three months of accelerated stability studies²⁴.

Ambroxol Hydrochloride: Ambroxol hydrochloride (HCl) is a very bitter drug and slightly soluble in water. Therefore to mask the taste and to formulate an orodispersible tablet by complexation with ion exchange resins, which also acts as super disintegrating agents a new dispersible formulation, was designed. Cation exchange resins like Indion-204 and Indion-234 were utilized for the sorption of the drug. Drug-

resinates were prepared in drug to resin ratio of 1:5 and 1:6. Tablets with both the resins have shown quick disintegrating features, *i.e.*, within 20 s, which is very characteristic of orodispersible tablets. Also, the dispersion not showing any bitter taste, indicate the capability of ion exchange resins used, both as taste masking and super disintegrating agents²⁵.

Meloxicam: The formulation of Meloxicam dispersible tablet (DT) was carried out using PEG 6000, PEG 8000, PEG 20000, Lutrol F-127, and β -cyclodextrin for the preparation of solid dispersion. Melting and solvent evaporation methods prepared these solid dispersions. Dissolution studies were performed for plain meloxicam, solid dispersions, and tablet formulations. Infrared spectroscopy and differential scanning calorimetry were performed to identify the physicochemical interaction between drug and carriers. Dispersible tablets and effervescent tablets were compared with a tablet containing a plain drug for dissolution profile. Dissolution of DT improved significantly in SD product (<95% in 1 min)²⁶.

Cefditoren: As direct compression method was failed to formulate dispersible tablet of Cefditoren Pivoxil so wet granulation method was used. In preliminary study different superdisintegrants croscarmellose sodium (CCS), sodium starch glycolate (SSG) and crospovidone were evaluated for weight variation, content uniformity, hardness, disintegration time, and friability of tablets. Microcrystalline cellulose: low-substituted hydroxypropyl cellulose ratio was optimized 8:2 in the whole experiment as it gives minimum disintegration time. Full factorial designs 3^2 was used to optimize the concentration of superdisintegrants (X1) and SLS (X2) which were selected as independent variables, and friability, disintegration time and % CDR was selected as the dependent variable. From response surface plot of disintegration time, % drug release after 15 min (Q15) and friability it was found that lower disintegration time of tablets could be obtained when X1 and X2 are kept at an optimum level. Stability study of the final batch showed no significant changes in tablet properties²⁷.

Lomefloxacin HCl: This dispersible formulation was designed to enhance patient compliance, and

provide a quick onset of action, increasing the solubility and masking its bitter taste. Complexing Lomefloxacin HCl enhanced taste masking and solubility with hydroxyl propyl β cyclodextrin (HP- β CD) by a solvent evaporation method. The prepared complex was further compressed into tablets by direct compression using different superdisintegrants like sodium starch glycolate, croscarmellose sodium, polyplasdone XL-10 in a different concentration such as 1%, 1.5%, 2% using aspartame as a sweetener and aerosil as a lubricant. The drug release from FDT increases with increasing the concentration of superdisintegrants and was found to be highest with formulation F6 containing 1.5% croscarmellose sodium and was considered to be the best formulation with release up to 100.68% in 45 min²⁸.

Cefixime Trihydrate: Cefixime trihydrate orally dispersible tablet was formulated using co-processed super disintegrants and comparative study with the marketed product. Cefixime trihydrate orally dispersible tablet was prepared by direct compression method using co-processed super disintegrants such as cross-povidone and sodium starch glycolate in different concentrations²⁹.

Celastrol: A suitable adsorbent of self-micro-emulsion was chosen to develop fine solid self-micro-emulsifying dispersible tablets for promoting the dissolution and oral bioavailability of Celastrol. Microcrystalline cellulose KG 802 was added as a suitable adsorbent into the optimized liquid celastrol-SMEDDS formulation to prepare the dispersible tablets by wet granulation compression method. The optimized formulation of celastrol-SMEDDS dispersible tablets was finally determined by the feasibility of the preparing process and redispersibility. The *in-vitro* study showed that the dispersible tablets could disperse in the dispersion medium within 3 min with the average particle size of 25.32 ± 3.26 nm³⁰.

Co-Amoxiclav 228 and 312 mg: Co-amoxiclav dispersible tablet was made by dry granulation method using super-disintegrants ingredients such as crospovidone, croscarmellose sodium, and sodium starch glycolate and effervescent materials such as citric acid and sodium bicarbonate. The mixed powder was tested in terms of

compressibility, particle size distribution, and powders flowability. Some tests were performed for determination of assay, content uniformity, hardness, and friability of tablet, weight variation, wetting time, water absorption ratio and disintegration of tablets. A formulation containing amoxicillin trihydrate, potassium clavulanate, citric acid, sodium bicarbonate, mannitol, aspartame and PEG 6000 had 25 sec disintegration time and 40N hardness³¹.

Paracetamol: The drug solubility was increased by solid dispersion method, in which two techniques namely physical mixing and co-grinding were tried at the ratios of 1:0.25, 1:0.5 & 1:0.75 for paracetamol to oats powder. Various parameters like pre & post compressional parameters were tested, and the final formula was selected based on disintegration time and *in-vitro* dissolution profile. All the formulations dispersed between 92 sec and showed 100% release at 20th min which was found to be faster as compared to the marketed formulation. The final formulation was prepared by the co-grinding technique, at 1:0.75 paracetamol to oats powder ratio using the direct compression method. The said formulation showed zero-order drug release, and mechanism of release is Super case - II transport ($n = 0.9738$)³².

Amoxicillin Trihydrate: Amoxicillin Trihydrate dispersible tablets were prepared by direct compression technique using microcrystalline cellulose (MCC) as directly compressible diluents. Sodium starch glycolate (SSG), croscarmellose sodium (CCS) and crospovidone used as synthetic superdisintegrants. The amoxicillin dispersible tablet powder blends showed satisfactory flow properties. Tablets prepared with the blend of CCS (15mg) and crospovidone (15mg) exhibited quicker disintegration. According to the present study, it was found that tablets of batch F4 (a blend containing CCS & crospovidone (15 mg)) showed the better disintegrating property as well as % drug release (98.78% within 40 min)³³.

Bacopa monnieri: The inclusion complex of *Bacopa monnieri* and β -cyclodextrin was prepared in different molar ratios of *Bacopa monnieri* by coprecipitation method. Phase solubility study was conducted to evaluate the effect of β -cyclodextrin on aqueous solubility of Bacoside A. The

characterization was determined by Fourier Transformation Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC) and X-ray Diffraction Study (XRD). Crospovidone and croscarmellose sodium were used as a super disintegrant. The 3² full factorial design was adopted to investigate the influence of two superdisintegrants on the wetting time and disintegration time of the tablets. The molar ratio (1:4) of inclusion complex enhance 3-fold solubility. A full factorial design was successfully employed for the optimization of the dispersible tablet of *B. monnieri*. The short-term accelerated stability study confirmed that the high stability of *B. monnieri* in inclusion complex³⁴.

Ganke Shuangqing: The Previous study showed that baicalin was less bitter than andrographolide. Thus, particle coating technology was adapted to prepare composite particles that baicalin coated on the surface of andrographolide to decrease bitterness. Initially, the particle size of baicalin and coating time of composite was investigated to prepare a composite. Then, scanning electron microscopy, wettability, and infrared (IR) spectrogram were used to characterize the microstructure of composite. Furthermore, the electronic tongue test, animal preference experiment, and human sensory test were applied to evaluate the masking effect. To produce a composite, baicalin should be ground in vibromill for 6 min. Then, andrographolide fine powder was added to grind together for 6 min. The contact angle of the composite was smaller than a mixture and more similar to baicalin. Other physical characterization including microstructure, wettability, and IR also suggested that andrographolide was successfully coated by baicalin superfine. Furthermore, the taste-masking test indicated taste-masked tablets were less bitter than original tablets.

The study indicated that particle coating technology could be used for taste masking of GKSQDT without adding other substance. Moreover, it provides a new strategy of taste masking for national medicine³⁵.

Rizatriptan Benzoate: The sweetener like aspartame was used in variable ratio with the drug. A physical mixture of Rizatriptan benzoate with

Aspartame (1:5 ratio) was rated most effective (0.4) by the panel of tastes. The other used sweeteners did not prove to be very effective for masking of a bitter taste as indicated by the high rating of bitterness score 2-3 and 3-4 by a panel of human tastes. Water-dispersible tablets of Rizatriptan benzoate was formulated by direct compression method using the physical mixture of drug: aspartame with superdisintegrants *viz.* sodium starch glycolate, croscarmellose sodium and crospovidone in variable ratios. The combination of sodium starch glycolate with crospovidone in the ratio of 1:2 given best result (disintegration time 19.18 sec), the disintegration time was decreased from 32 to 19 sec³⁶.

Deacetylmucoepoxydience: A novel nano-crystal dispersible tablets was developed by apply quality by design (QbD) approach. Following the Diacetyl Mycoepoxydience (DM) nanosuspensions was prepared by the anti-solvent precipitation approach; the DM nano-crystal was solidified by the freeze-drying method. Following the screening of cryoprotectants for solidification of the nanosuspensions, the physicochemical properties including re-dispersibility, mean particle size (MPS), morphology and dissolution behavior of the DM nano-crystal was investigated.

The experiment was designed with a focus on the types and quantities of the disintegrating agent during the DM nano-crystal dispersible tablets preparation. The DM nano-crystal loaded dispersible tablets were produced using direct powder compression. Judging from the tablet disintegration time, central composite design (CCD) and response surface methodology were adopted to optimize disintegrating agent. In conclusion, the nano-crystal dispersible tablets approach was a reliable method for improving the dissolution and thereby the oral bioavailability of the DM in formulation development³⁷.

CONCLUSION: There are many gaps in our knowledge about pediatric formulations and many challenges for industry to face if suitable preparations are to be available for all age ranges. These include acceptable dose volumes and sizes; safety, e.g., risk of aspiration or choking for solid dosage forms; excipients acceptability; taste (and how best to assess during development).

An ideal formulation for children will allow minimal dosage and frequency; will have one dosage form to fit all or a full range; will have minimal impact on lifestyle; a minimum of non-toxic excipients and will have convenient, easy, reliable administration. It should also be easily produced, elegant, stable, cheap and commercially viable. The challenge in achieving this should not be underestimated.

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