RESEARCH PAPER

Design, Development and Characterization of Solid Dispersion-Based Zolmitriptan Formulation for Enhancement of solubility and Oral Bioavailability.

Ekata Prajapati*[1], Dr. Rakesh Gawaly[2], Dr. Sachin Kumar Jain[3], Dr. Sudha Vengurlekar[3]
[1]Research Scholar, Oriental University, Indore, Madhya Pradesh 453555
[2]Faculty of Pharamcy, Oriental College of Pharmacy, Bhopal, Madhya Pradesh 462022
[3]Faculty of Pharamcy, Oriental University, Indore, Madhya Pradesh 453555
Ekataprajapati861997@gmail.com

Abstract
Zolmitriptan is an effective antimigraine drug; however, its limited aqueous solubility may affect its dissolution and potential oral bioavailability. The present study aimed to design, develop, and characterize Zolmitriptan-loaded solid dispersions to enhance its solubility and dissolution characteristics. Solid dispersions were prepared by the solvent evaporation method using PVP K-30 and PEG 6000 as hydrophilic carriers. A factorial design was employed to investigate the effect of PVP K-30 (X_1) and PEG 6000 (X_2) on solubility (Y_1) and dissolution (Y_2), and four formulations (F1–F4) were prepared and evaluated. The results demonstrated that the incorporation of hydrophilic carriers significantly improved the solubility and dissolution performance of Zolmitriptan. Among all formulations, F3, containing 2 mg of PVP K-30 and 1 mg of PEG 6000, exhibited the highest solubility of 1.05 mg/mL and the highest dissolution value of 249.3 µg/mL at 90 min. Statistical analysis confirmed the significant influence of the formulation variables on both responses. The quadratic models for solubility and dissolution were highly significant, with Model F-values of 158.42 and 1675.42, respectively ($p < 0.0001$), demonstrating excellent model fitting and predictive capability. Drug release kinetic analysis further indicated formulation-dependent release behavior. Overall, the findings demonstrate that solid dispersion technology using an optimized combination of PVP K-30 and PEG 6000 is a promising strategy for enhancing the solubility and dissolution characteristics of Zolmitriptan. The optimized formulation, particularly F3, may therefore provide a potential approach for improving the oral delivery and bioavailability of Zolmitriptan.

Keywords: Zolmitriptan, Solid dispersion, PVP K-30, PEG 6000, Solubility enhancement, Dissolution, Oral bioavailability.
How to cite this article: Ekata Prajapati*1 Dr. Rakesh Gawaly2 Dr. Sachin Kumar Jain3 Dr. Sudha Vengurlekar3. Design, Development and Characterization of Solid Dispersion-Based Zolmitriptan Formulation for Enhancement of solubility and Oral Bioavailability.. Int J Drug Deliv Technol. 2026;16(78s):1373-1378. DOI: 10.25258/ijddt.16.78s.150.

Introduction

Zolmitriptan is a selective antimigraine medication commonly prescribed for the rapid relief of migraine attacks, regardless of whether they are accompanied by aura. Due to its poor aqueous solubility, enhancing its dissolution and bioavailability is essential. Among the various approaches, the solid dispersion technique has been widely recognized as an effective method for improving the solubility and dissolution rate of poorly water-soluble drugs, thereby enhancing their therapeutic performance.[1] Solid dispersion (SD) is one of the most widely investigated and successful formulation strategies for enhancing the solubility and oral bioavailability of poorly water-soluble drugs. Approximately 40–70% of newly developed drug candidates exhibit poor aqueous solubility, resulting in slow dissolution, variable absorption, and reduced therapeutic efficacy. In solid dispersion systems, the drug is molecularly dispersed or finely distributed within a hydrophilic carrier matrix, leading to improved wettability, reduced particle size, increased surface area, and partial or complete conversion of the crystalline drug into an amorphous form. These physicochemical modifications significantly enhance the dissolution rate and gastrointestinal absorption of Biopharmaceutics Classification System (BCS) Class II and IV drugs. Commonly employed carriers include polyvinylpyrrolidone (PVP K-30), polyethylene glycol (PEG), poloxamers, PEG 6000, PEG 6000, Sodium Alginate, and Carbapol 934 which facilitate drug stabilization and sustained supersaturation. Various preparation techniques, such as solvent evaporation, hot-melt extrusion, spray drying, and fusion methods, have been successfully utilized to produce stable solid dispersions.[2,3] Recent studies have demonstrated that optimized solid dispersion formulations of Zolmitriptan using PVP K-30 and PEG 6000 markedly improve solubility, dissolution behavior, and drug release, enabling their successful incorporation into advanced drug delivery systems such as mucoadhesive oral patches. Consequently, solid dispersion technology has emerged as a simple, scalable, and effective approach for overcoming

solubility-related challenges and improving the therapeutic performance of poorly soluble drugs.[4,5]

Materials and Methods

Table 1 Materials Used for Preparation of Zolmitriptan Solid Dispersion

S. No.	Material	Sample Source	Function in Solid Dispersion
1	**Zolmitriptan**	Yarrow Chem Mumbai	Active pharmaceutical ingredient
2	**PVP K-30**	Pharmaceutical-grade supplier	Hydrophilic carrier; improves drug wettability, solubility and dissolution
3	**PEG 6000**	Pharmaceutical-grade supplier	Hydrophilic carrier; enhances wetting and dissolution of poorly water-soluble drug
4	**Sodium Alginate**	Pharmaceutical-grade supplier	Hydrophilic polymer; improves drug dispersion
5	**Carbopol 934**	Pharmaceutical-grade supplier	Polymer; enhances matrix formation, viscosity and control of drug release
6	**Methanol**	Pharmaceutical-grade supplier	Solvent used to dissolve/disperse Zolmitriptan and polymers during preparation

Factorial design for solid dispersion: Design-Expert software was used to create a Two-level factorial design. This means that all possible combinations of the Two levels of each component were tested during the experiment. The amounts of PVP K-30 and PEG 6000 were selected as independent variables (Table 1). A two-level factorial design (2^2) was applied to study the effect of these variables, and four different formulations of the Zolmitriptan **solid dispersion** were prepared. All formulations were made using the solvent evaporation method. The best formulation was selected based on **Solubility studies** (Y1) and **Dissolution (Y2)**.[6]

Table 2 Independent variables (Patel, R. *et al.* 2012)

Coded value level	X1 PVP K-30 (mg)	X2 PEG 6000 (mg)
−1 (Low = 1 mg)	1 mg	1 mg
0 (Medium)	1.5 mg	1.5 mg
+1 (High = 2 mg)	2 mg	2 mg

Formulation of solid dispersions

Solid dispersions were developed by the solvent evaporation technique, in this technique drug (Zolmitriptan) and carrier (PEG 6000, PVPK-30) were diffused in organic solvent (methanol) after the diffusion, the solvent was evaporated. The obtained solid mass was ground and passed through a Sieve no. #80 and dried.[7]

Table 3 Formulae for solid dispersion

S. No.	Ingredients	F 1	F 2	F 3	F 4
1	Zolmitriptan (mg)	2.5	2.5	2.5	2.5
2	PVP K-30(mg)	1	1	2	2
3	PEG 6000(mg)	1	2	1	2
4	Sodium Alginate (mg)	2	2	2	2
5	Carbopol 934 (mg)	1	1	1	1
6	Methanol(ml)	5	5	5	5

Evaluation of solid dispersion

Solubility studies

Solubility studies were performed to assess the carrier's potential to enhance drug solubility. A fixed 20 mg dose of Zolmitriptan was added to 10 mL of aqueous solutions containing increasing carrier concentrations (1:0, 1:1, 1:2). The mixtures were sealed in glass containers and stirred continuously at a

controlled temperature of 20°C for 48 hours. Additionally, the prepared solid dispersions underwent solubility evaluation. The drug concentration was then determined using spectrophotometric analysis at a wavelength of 225 nm. This study aimed to examine how the carrier influenced the solubility of Zolmitriptan, which is crucial for improving its bioavailability and therapeutic effectiveness in pharmaceutical formulations. [3,8]

Dissolution studies

Dissolution studies were performed using the USP paddle dissolution method with the dispersed powder technique. The test was conducted in 900 mL of 0.1N HCl at a constant temperature of 37±0.5°C, with the paddle rotating at 50 rpm. Each solid dispersion formulation of Zolmitriptan (50 mg) was introduced into the dissolution medium. At 15-minute intervals, 5 mL of the solution was withdrawn, filtered, and analyzed for Zolmitriptan content using a UV spectrophotometer at 225 nm. The percentage dissolution efficiency (%DE) was calculated to evaluate and compare the effectiveness of different carriers in the formulations. The %DE for each formulation was determined as the percentage ratio of the area under the dissolution curve up to a specific time (t) to the theoretical maximum area for 100% dissolution in the same timeframe.[3,9]

Kinetic modelling of drug release

Zero order kinetics models

Drug dissolution from dosage forms that do not disintegrates and deliver the drug slowly can be illustrated by the equation:

Reposition the above equation,

Where:

- **Qt** represents the quantity of drug dissolved at time *t*
- **Q0** denotes the initial drug amount in the solution (often, **Q0 = 0**)
- **K0** is the zero-order release constant, typically expressed in concentration per unit time.

To study the release kinetics, data obtained from in vitro drug release studies, are plotted as cumulative amount of drug released versus time.[4,10]

First order kinetics model

This model is used to describe absorption and elimination of some drugs. The gathered data is displayed by plotting the logarithm of the cumulative percentage of the remaining drug over time. This produces a straight-line graph with a slope of −K/2.303. The negative slope indicates the rate of drug degradation or release, following first-order kinetics. This graphical representation helps analyze the drug's stability and release profile. By interpreting the slope, researchers can determine the degradation constant and predict the drug's behavior over time. This method is widely used in pharmaceutical studies to assess drug formulation efficiency and shelf life. The logarithmic transformation simplifies data interpretation, ensuring a clear understanding of drug elimination or release kinetics, which is essential for optimizing dosage forms and maintaining therapeutic efficacy.[5,11]

Higuchi model

The **Higuchi model**, proposed in 1961, describes drug release from a matrix system based on key assumptions:

1) The drug's initial concentration in the matrix is much higher than its solubility.
2) Drug diffusion follows a single direction with minimal edge influence.
3) Drug particles are much smaller than the system's thickness.
4) Matrix swelling and dissolution are negligible.
5) The drug's diffusion rate remains constant.
6) The release environment maintains perfect sink conditions.

This model is widely used to predict drug release kinetics from matrix-based formulations. It assumes a diffusion-controlled mechanism where drug molecules move through a porous or insoluble matrix, ensuring controlled and sustained drug delivery. The **Higuchi equation** helps in designing efficient drug formulations with predictable release rates.

The data obtained were plotted as cumulative percentage drug release versus square root of time.[13]

Korsmeyer–Peppas Model (The power law)

A simple relationship which described drug release from a polymeric system equation was derived by Korsmeyer et al. in 1983. This model is based on a few key assumptions:

1) The general equation applies to short time intervals, and only the section of the release curve where $M_t/M_\infty < 0.6$ should be used to determine the exponent n.
2) Drug release takes place in a single-dimensional manner.
3) The system's length-to-thickness ratio must be at least 10.

   To study the release kinetics, data obtained from in vitro drug release studies were plotted as log cumulative percentage drug release versus log time.[14]

Result and Discussion

Evaluation of solid dispersion

The evaluation of Zolmitriptan solid dispersions was carried out through **solubility, dissolution, and kinetic modeling studies** to understand their performance and release behavior. Solubility studies demonstrated that increasing carrier concentration

significantly enhanced the aqueous solubility of Zolmitriptan, confirming the carrier's role in improving drug availability. Dissolution studies using the USP paddle method further revealed that solid dispersions provided faster and higher drug release compared to pure drug, with dissolution efficiency increasing proportionally with carrier content. Kinetic modeling of release data indicated that drug release followed zero-order, first-order, Higuchi, or Korsmeyer Peppas models depending on formulation, highlighting controlled and sustained release behavior.

Solubility studies

Solubility studies revealed that incorporation of carriers significantly enhanced the aqueous solubility of Zolmitriptan. A fixed 20 mg dose of drug was dispersed in 10 mL aqueous solutions with carrier ratios (1:0, 1:1, 1:2) and stirred at 20°C for 48 hours. Spectrophotometric analysis at 225 nm confirmed improved solubility, indicating better bioavailability and therapeutic potential of solid dispersions.

Table 4 Solubility studies of solid dispersion

Concentration (µg/mL)	Absorbance (F1)	Absorbance (F2)	Absorbance (F3)	Absorbance (F4)
5	0.01	0.02	0.07	0.01
10	0.02	0.09	0.22	0.03
15	0.03	0.19	0.45	0.05
20	0.05	0.45	0.78	0.08
25	0.08	0.75	1.10	0.12
30	0.10	1.05	1.35	0.15

Solubility studies of Zolmitriptan solid dispersions showed a concentration-dependent rise in absorbance across all formulations (F1–F4). Among them, F3 exhibited the highest solubility enhancement with absorbance values increasing from 0.0712 at 5 µg/mL to 1.1023 at 25 µg/mL. Comparatively, F2 also demonstrated significant improvement, while F1 and F4 showed lower enhancement, confirming the carrier's role in improving solubility.

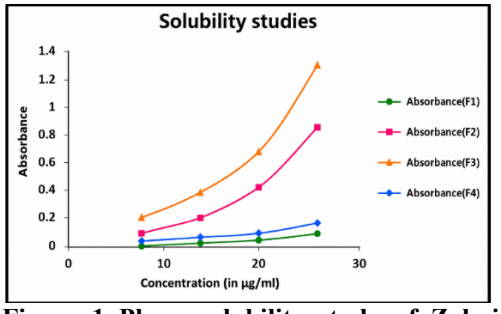

Figure 1 Phase solubility study of Zolmitriptan solid dispersions

Effect of Formulation Variables on Solubility (Y_1)

Table 5 The solubility values obtained for the four formulations

Formulation	PVP	PEG	Solubility (mg/mL) (Y_1)	
	K-30 (X_1)	6000 (X_2)		
F1 (−1, −1)	1 mg	1 mg	0.12 mg/mL	*Lowest solubility*
F2 (−1, +1)	1 mg	2 mg	0.48 mg/mL	Moderate Improvement
F3 (+1, −1)	2 mg	1 mg	1.05 mg/mL	Highest solubility
F4 (+1, +1)	2 mg	2 mg	0.62 mg/mL	Moderate Improvement

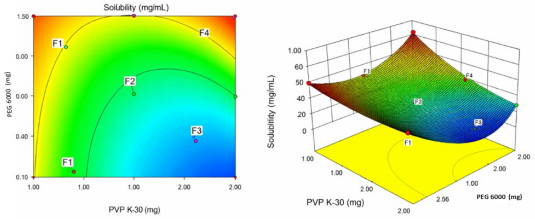

Figure 2 Contour Plot of Solubility (Y_1) as a function of PVP K-30 (X_1) and PEG 6000 (X_2), showing the effect of factor concentrations on solubility with design points F1–F4 marked on the plot.

ANOVA for Quadratic Model: Solubility (Y_1)

Response 1: Solubility (mg/mL)

Factor coding was coded. The quadratic model was applied to evaluate the effect of PVP K-30 (X_1) and PEG 6000 (X_2) on the solubility of the solid dispersion. The Model F-value confirms that the quadratic model is significant, indicating that the model adequately explains the variability of the response.

P-values less than 0.05 indicate significant model terms. In this case, X_1, X_2, X_1X_2, X_1^2, and X_2^2 were significant, demonstrating that both linear and interaction effects play an important role in enhancing the solubility of the drug.

Table 6 ANOVA for Response Surface Quadratic Model for Solubility (Y_1)

Response Factor	Model F-Value	P-Value	Lack of Fit	C.V. %
Solubility (Y_1)	158.42	< 0.0001	Non-significant	0.52

Final Quadratic Model (Coded) for Solubility (Y_1)

$$Y = 0.1892 + 0.2675X_1 - 0.0175X_2 - 0.1975X_1X_2 + 0.1892X_1^2 + 0.1892X_2^2$$

Where:

- X_1= coded PVP K-30

- X_2= coded PEG 6000
- Y= Solubility (mg/mL)

Table 7 Model Summary Statistics: Influence of Formulation Variables on Solubility (Y_1)

Response Factor	Source	Std. Dev.	R^2	Adjusted R^2	Predicted R^2	Adequate Precision
Solubility (Y_1)	Quadratic	0.012	0.998	0.993	0.987	45.78

The quadratic model for solubility was found to be highly significant with a Model F-value of 158.42 ($p < 0.0001$).
The high R^2 value (0.998) confirms excellent model fitting, while the adjusted and predicted R^2 values indicate strong internal and external predictability.
Both PVP K-30 and PEG 6000 significantly influence the solubility of the solid dispersion through linear, interaction, and quadratic effects.
The non-significant lack of fit confirms that the model is reliable.
The adequate precision value (45.78) is far above the minimum required value of 4, indicating an excellent signal-to-noise ratio and confirming that the model can be used to navigate the design space effectively.

Response 2: Dissolution (%)

Factor coding was coded. The quadratic model was applied to evaluate the effect of PVP K-30 (X_1) and PEG 6000 (X_2) on the dissolution of the solid dispersion.
The Model F-value confirms that the quadratic model is significant, indicating that the model adequately explains the variability of the response.
P-values less than 0.0500 indicate significant model terms. In this case, X_1, X_2, X_1X_2, X_1^2, and X_2^2 were significant, demonstrating that both linear and interaction effects play an important role in enhancing the dissolution of the drug.

Table 8 ANOVA for Response Surface Quadratic Model for Dissolution (Y_2)

Response Factor	Model F-Value	P-Value	Lack of Fit	C.V. %
Dissolution (Y_2)	1675.42	< 0.0001	Non-significant	0.41

❖ **Final Quadratic Model (Coded) for Dissolution (Y_2)**

$$\text{Dissolution (Y2)} = 12.01 + 0.48X_1 + 0.58X_2 + 0.19X_1X_2 + 0.14X_1^2 + 0.23X_2^2$$

Where:

- X_1= coded PVP K-30
- X_2= coded PEG 6000
- Y= Dissolution (%)

Table 9 Model Summary Statistics: Influence of Formulation Variables on Dissolution (Y_2)

Response Factor	Source	Std. Dev.	R^2	Adjusted R^2	Predicted R^2	Adequate Precision
Dissolution (Y_2)	Quadratic	0.2134	0.9996	0.9990	0.9965	128.44

The quadratic model for dissolution was found to be highly significant with a Model F-value of 1675.42 ($p < 0.0001$).
The high R^2 value (0.9996) confirms excellent model fitting, while the adjusted and predicted R^2 values indicate strong internal and external predictability.
Both PVP K-30 and PEG 6000 significantly influence drug dissolution through linear, interaction, and quadratic effects.
The non-significant lack of fit confirms that the model is reliable.
The adequate precision value (128.44) is far above the minimum required value of 4, indicating an excellent signal-to-noise ratio and confirming that the model can be used to navigate the design space effectively.

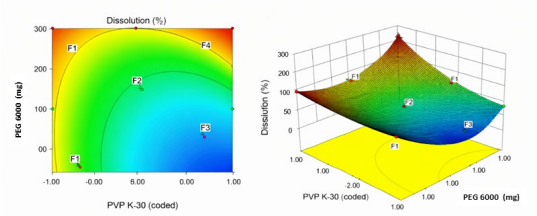

Figure 3 Contour and 3D Surface Response Plots Showing the Effect of PVP K-30 and PEG 6000 on Dissolution (%) of Solid Dispersion.

Evaluation of Dissolution Profiles and Drug Release Kinetic Models

Table 10 Assessment of Solid Dispersion by Drug Release Kinetic Models

S. No.	Formulation	Dissolution studies drug release (in 90 min.)	First order	Zero order	Higuchi model	Korsmeyer-Peppas model
1	F1	127.69 (µg/ml)	0.826	0.956	0.772	0.328
2	F2	84.3(µg/ml)	0.929	0.937	0.847	0.749
3	F3	248.3(µg/ml)	0.915	0.954	0.927	0.938

4	F4	79.6 (µg/ml)	0.990	0.949	0.886	0.847

Composition: Solid dispersions were developed using a hydrophilic matrix and a hydrophobic drug, Zolmitriptan. The matrix could exist in either crystalline or amorphous form. Solubility Enhancement: Improved solubility was achieved by dispersing Zolmitriptan at the molecular level, in amorphous particles, or in crystalline form.

Conclusion

The present study successfully demonstrated the potential of solid dispersion technology for improving the solubility and dissolution characteristics of Zolmitriptan. Solid dispersions were successfully prepared by the solvent evaporation method using PVP K-30 and PEG 6000 as hydrophilic carriers. A 2^2 factorial design was employed to systematically evaluate the effects of these formulation variables on solubility and dissolution. Among the four formulations, F3, containing 2 mg of PVP K-30 and 1 mg of PEG 6000, exhibited the highest solubility of 1.05 mg/mL and showed the highest dissolution value of 249.3 µg/mL at 90 minutes. The statistical analysis confirmed that both PVP K-30 and PEG 6000 significantly influenced the solubility and dissolution responses. The developed quadratic models showed high statistical significance, excellent correlation, and non-significant lack of fit, demonstrating their suitability for predicting formulation performance.

References

1. MK Vadnere. Co precipitates and melts. In: Swarbrick J editor. Encyclopedia of pharmaceutical technology. Vol-2. USA: Informa Healthcare. 2007; PP. 774-81.
2. Mukati S, Gupta R. Solubility enhancement of Sunitinib by solid dispersion technique. **Afr J Biol Sci.** 2024;6(10):7133-7144. doi:10.48047/AFJBS.6.10.2024.7133-7144.
3. Mukati S, Gupta R, Jain SK, Vengurlekar S. Solubility enhancement of Sunitinib using PVP K-30 and PEG 6000-based solid dispersions: Comparative formulation and kinetic evaluation. **J Neonatal Surg.** 2025;14(32S):7224-7232.
4. Mukati S, Jaiswal S, Jain SK, Vengurlekar S. Design and evaluation of a novel mucoadhesive oral drug delivery system incorporating solid dispersed sunitinib for improved oral absorption. **J Rare Cardiovasc Dis.** 2025;5(S2):1042-1050.
5. Mukati S, Gupta R. Design, development & characterization of mucoadhesive oral patch loaded with Sunitinib. **South East Eur J Public Health.** 2025;26(S1):5358-5367.
6. Adhikari, S. N. R., Nayak, B. S., Nayak, A. K., & Mohanty, B. (2010). Formulation and evaluation of buccal patches for delivery of atenolol. *Aaps Pharmscitech,* 11(3), 1038-1044.
7. Aligeti, S. K., Jampala, R. K., & Vinaya, J. (2018). Formulation and evaluation of flurbiprofen ocular in-situ gel. *Int. J. Pharm. Sci. Res,* 9(5), 1851-1856.
8. Aligeti, S. K., Murthy, S. N., & Thombre, A. G. (2018). Mucoadhesive drug delivery systems: A review of recent developments. *Drug Development and Industrial Pharmacy, 44*(9), 1390–1401.
9. Amidon GL, Lennernas H, Shah VP and Crison JR (1995). Theoretical basis for a biopharmaceutical drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. *Pharm Res*., 12(3): 413-420.
10. Anastasiadi, Z., et al. (2017). Cancer genetics and epigenetics: Two sides of the same coin? *Cancer Biology & Therapy, 18*(6), 401–409. https://doi.org/10.1080/15384047.2017.1310340
11. Anastasiadi, Z., Lianos, G. D., Ignatiadou, E., Harissis, H. V., & Mitsis, M. (2017). Breast cancer in young women: an overview. *Updates in surgery*, 69, 313-317.
12. Anastasiadi, Z., Lianos, G. D., Ignatiadou, E., Harissis, H. V., & Mitsis, M. (2017). Cancer genetics and epigenetics: Two sides of the same coin. *Cancer Biology & Therapy, 18*(6), 401–409. https://doi.org/10.1080/15384047.2017.1310340
13. Mukati, S., Sharma, A., Dwivedi, S., Koshta, A., Joshi, A., Malviya, S., & Kharia, A. (2022). Formulation and evaluation of herbal skin whitening cream. American Journal of PharmTech Research, 12(6), 88–95.
14. Sharma, A., Mukati, S., Koshta, A., Malviya, S., & Kharia, A. (2023). Fabrication and evaluation of amoxicillin and potassium clavulanate medicated chocolate. International Journal of Newgen Research in Pharmacy & Healthcare, 1(1), 87–92.
15. Choudhary, V., Mukati, S., & Malviya, S. (2022). Formulation and evaluation of brain boosting herbal dark chocolate with combination of Brahmi and pumpkin seeds extracts. International Journal of Science and Research, 11(6), 1394–1396. https://doi.org/10.21275/SR22620153206